The role of disease severity and illness perceptions in predicting quality of life and symptoms of anxiety and depression in people with hidradenitis suppurativa a longitudinal study

Jones, Kelsey

Awarding institution:
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Systematic Literature Review
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Kelsey Jones

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Institute of Psychiatry, Psychology, and Neuroscience
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Volume Contents

PART I

Systematic Review

Anxiety, Depression and Quality of Life in Hidradenitis Suppurativa: A Systematic Literature Review

Supervised by Professor John Weinman and Dr Mark Turner

Institute of Psychiatry, Psychology, and Neuroscience

King's College London

Table of Contents

List of Tables

List of Figures

Abstract

Background: Research indicates that hidradenitis suppurativa (HS) can have a significant psychosocial impact on individuals, with a range of factors found to be associated with outcomes. Systematic reviews to date have explored anxiety, depression and quality of life in other dermatological diseases, however there has only been one which focuses on prevalence of anxiety and depression in HS. The aim was to systematically review the prevalence of anxiety, depression and poor quality of life in HS, and any associated factors. Findings informed the development of recommendations for assessment and interventions in HS, and areas for future research.

Method: Databases that were searched included EMBASE, MEDLINE, PsychINFO using Ovid, PubMed, Cumulative Index to Nursing and Allied Health Literature, Web of Science and three grey literature databases. Search terms regarding anxiety, depression and quality of life in people with HS were used, papers retrieved were screened according to inclusion/exclusion criteria.

Results: Twenty-three studies were eligible for inclusion in the review. Nineteen papers assessed quality of life, whereas eight measured depression and three measured anxiety. Prevalence rates of anxiety, depression and poorer quality of life were found to be higher than control groups including other skin diseases and the general population. Prevalence rates were 27% for anxiety, between 5.5% and 38.6% for depression, and quality of life was within the ranges of moderate to very large impact. Several factors were associated with these outcomes including demographic, psychosocial, lifestyle and clinical factors. The methodological quality for most studies was rated as fair, three were good and seven were poor. But these findings were not related to prevalence rates/main outcome data.

Conclusions: The findings of this review suggest that routine assessments of people with HS may benefit from inclusion of anxiety, depression and quality of life measures, in addition to measures of factors found to be associated with these psychosocial outcomes. These may include illness beliefs, sexual function, disease severity and pain. It will be useful for future research to focus on developing psychological interventions to support people with HS who are at risk of or are experiencing poor health outcomes, and target factors such as illness perceptions and sexual dysfunction. Further research is required using longitudinal and cohort study designs to identify factors that are predictive of poorer health outcomes and inform earlier intervention.

1. Introduction

Hidradenitis suppurativa (HS) is a chronic, painful and debilitating inflammatory dermatological disease of the apocrine glands (groin, armpits and anogenital areas), which presents as malodorous abscesses, nodules, fistulas and scarring (Dhaou, Boussema, Aydi, Baili & Rokbani, 2013). The global prevalence rate is 1 - 4% (3:1 ratio of women to men), with the average age of onset being in early twenties and remaining typically active during the thirties and forties (Dufour, Emtestam & Jemec, 2014). Currently there is no cure for HS, and dermatological treatment is dependent on disease severity (Elkin, Daveluy & Avanaki, 2020). There are a number of different HS severity measures that are used clinically and in research including Hurley staging (Hurley, 1989), Modified Sartorius Score (Sartorius, Emtestam, Jemec & Lapins, 2009; Sartorius, Lapins, Emtestam & Jemec, 2003), HS-Physician's Global Assessment (HS-PGA; Kimball et al., 2012; Zouboulis et al.., 2015), Hidradenitis Suppurativa Clinical Response (HiSCR; Kimball et al., 2016), and International Hidradenitis Suppurativa Severity Scoring System (Kimball et al., 2014; Scuderi et al, 2017; Zouboulis et al., 2017).

Research has indicated that HS can have a significant psychosocial impact. Indeed, lesions often result in soreness and pain as well as feelings of shame and embarrassment, which can lead to higher rates of sick leave than the general population and impaired quality of life (Alikhan, Lynch & Eisen, 2009). Quality of life (QoL) can be defined using different terms, such as wellbeing, functioning and health-related quality of life and measured using a range of tools with varying constructs. Research into dermatological diseases such as psoriasis and HS are increasingly using standardised quality of life screening tools that measure constructs including psychological, physical and social functioning (de Korte, Sprangers, Mombers & Bos, 2004; Kofler et al., 2018). A validated measure that has been used widely in dermatological research and clinical use is the Dermatology Quality of Life Index (DLQI; Finlay & Khan, 1994), which has ten items each with cut-off points (Hongbo, Thomas, Harrison, Salek and Finlay, 2005) indicating no effect on patient's life (0 - 1), small effect (2 - 5), moderate effect (6 - 10), very large effect (11 - 20), extremely large effect (21 - 30). Another common measure is the Skindex-29 (Chren, Lasek, Flocke & Zyanski, 1997), which has three domains assessing symptoms, emotions and functioning; each domain has a cut-off to establish

severe impairment. Higher prevalence of impaired quality of life has been found in people with HS, compared to other dermatological diseases such as psoriasis and atopic dermatitis (Gooderham & Papp, 2015; Kohorst, Kimball & Davis, 2015; Wolkenstein, Loundou, Barrau & Auquier, 2007). This review will consider quality of life in the context of participants' subjective ratings of the impact that HS has on their wellbeing, using validated quality of life questionnaires to enable comparisons with other studies and populations.

Higher prevalence of anxiety and depressive symptoms has also been found in HS, compared to the general population (Onderdijk et al., 2013; Shavit et al., 2015), and more common in females than males (Shavit et al., 2015). The World Health Organisation (WHO, 2017) reported that the point prevalence rate of anxiety disorders globally was estimated to be 3.6% in 2015, and more common among females (4.6%) than males (2.6%). Prevalence of anxiety in people with HS was found to be higher than this at 4.9% in a recent systematic review and meta-analysis by Machado et al. (2019), and 6.9% in a nationwide Finnish study of 4381 people with HS (Huilaja, Tiri, Jokelainen, Timonen & Tasanen, 2018). In Huilaja et al.'s (2018) study the prevalence of anxiety was also higher in HS than in people with psoriasis (5%) and melanocytic nevi (3.8%, the control group).

In terms of depression, prevalence rates vary widely across studies in the general population. Globally in 2015 the point prevalence was estimated to be 4.4%, and also more common among females compared to males (WHO, 2017). However, a meta-analysis between 1994 and 2014 across 30 countries found an aggregate point prevalence of 12.9% (Lim et al., 2018). Variable findings are also evident in research of people with HS. A population-based study by Vazquez, Alikhan, Weaver, Wetter and Davis (2013) found 43% of 268 participants with HS were diagnosed with depression. Machado et al. (2019) found that across 10 studies of HS, the prevalence of depression was 16.9%, however this was 26.8% in studies that used a screening instrument. These findings suggest that there may be a higher prevalence of depression in people with HS than the general population, but that this could be over or underestimated based on the methods used to assess this.

Depressive symptoms have been found to be more prevalent in HS than other dermatological diseases (Onderdijk et al., 2013). In Huilaja et al.'s (2018) nationwide

study, major depression was more common in HS (15.3%) compared to the psoriasis group (12.1%) and melanocytic nevi group (8.3%). It should be noted however that depression prevalence in psoriasis has also been found to vary broadly, ranging from 4% to 68% in three systematic reviews (Daudén et al., 2013; Dowlatshahi, Wakkee, Arends & Nijsten, 2014; Roque Ferreira, Pio-Abreu, Reis & Figueiredo, 2017), which can make this more difficult when comparing prevalence to HS. Differences in prevalence rates of psoriasis may also be due to the method of assessment, for example Dowlatshahi et al.'s (2014) systematic review found a 15% difference in prevalence of depression between the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock & Erbaugh, 1961) and the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983).

There are various factors that may contribute to prevalence of anxiety, depression and poor quality of life in HS. Specific locations of lesions (head, nape and anogenital areas) have been linked with internal stigma, low self-esteem and impaired quality of life (Matusiak et al., 2010). A qualitative study of the psychosocial impact of HS indicated that people with HS reported experiencing feelings of being unworthy, helpless, unattractive and having a lack of control over their illness (Esmann & Jemec, 2011). Research across 13 European countries and numerous skin diseases including HS, also found that 23.1% reported sexual problems and that this was linked with anxiety, depression and suicidal ideation (Sampogna et al., 2017).

Impaired quality of life and depression have also been shown to be positively correlated with level of severity of HS, duration, pain, and more lesion locations (Alavi, Anooshirvani, Kim, Coutts & Sibbald, 2015; Kurek, Peters, Sabat, Sterry & Schneider-Burrus, 2013; Matusiak, et al., 2010; Wolkenstein et al., 2007). There is research debating the role of proinflammatory cytokines in impacting the development of mood disorders, including depression (Goldstein, Kemp, Soczynska & McIntyre, 2009; Kohler et al., 2017). The same cytokines have been found to be involved in the development of HS (Huilaja et al., 2018; Kelly & Prens, 2016; van der Zee et al., 2011). Notwithstanding, there has been considerable variation in the extent to which disease severity correlates with outcomes such as depressive symptoms, anxiety and quality of life (Pavon Blanco, Turner, Petrof & Weinman, 2018; Onderdijk et al., 2013). There has been increasing evidence to show that illness perceptions across various chronic illnesses (including psoriasis, heart failure, rheumatoid arthritis and chronic obstructive pulmonary disease)

are also significantly related to quality of life, anxiety and depression in addition to disease severity (Scharloo et al., 1998, 2000). Illness perceptions are cognitive models of illness including beliefs about cause, timeline, control or cure, consequences and identity (Petrie & Weinman, 2006). Pavon Blanco et al. (2018) recently found that illness perceptions about HS were more strongly associated with depression, anxiety and quality of life than disease severity. This finding suggests that psychological factors may be important to consider when assessing HS and its impact on quality of life, depression and anxiety, independently of the clinical presentation of HS.

Review Aims

Systematic reviews to date have explored the prevalence of depression, anxiety and quality of life in other dermatological diseases (de Korte et al., 2004; Dowlatshahi et al., 2014) and Rosacea (Krasuska, Millings, Lavda & Thompson, 2015). There is currently only one systematic review that has evaluated the prevalence of depression and anxiety in adults with HS (Machado et al., 2019). To the best of the author's knowledge, there is not a formal systematic review or ongoing reviews to summarise the available self-reported data from validated screening tools in terms of prevalence of anxiety, depression and quality of life in HS, and related factors. There were also no ongoing systematic reviews in line with this research question registered on the international Prospective Register of Systematic Reviews (PROSPERO). This review may indicate areas to develop in routine assessment and interventions of people with HS. Therefore, the main aims of this systematic review are as follows:

- To assess the prevalence of anxiety, depression and poor quality of life in HS.
- To consider what factors are associated with anxiety, depression and quality of life in people with HS.

2. Method

2.1 Search Strategy

The search was conducted in line the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher, Liberati, Tetzlaff, Altman & PRISMA Group, 2009) using the following six databases: EMBASE (Ovid), MEDLINE

(Ovid), PsychINFO (Ovid), PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Web of Science. The search strategy comprised of four components:

1. "Hidradenitis Suppurativa" OR "Hidradenitis" OR "Acne Inversa"
   AND
2. "Anx*" OR "Anxiety adj disorder$"
   OR
3. "Mood" OR "Depress*" OR "Mood adj disorder$" OR "Depress* adj disorder$" OR "distress"
   OR
4. "Quality adj2 life" OR "Life adj quality" OR "HRQL" OR "QoL" OR "Well adj being" OR "Well-being" OR "Wellbeing" OR "functioning"

Search limits of papers published between 1990 – current and published in English language were added to each database search. Searches of grey literature databases (unpublished literature such as doctoral dissertations and conference reports) using OpenGrey, EthOS and WorldCat, and manual searches of reference sections in retrieved studies were also performed (see Appendix A). The search on EMBASE, MEDLINE, PsychINFO and PubMed was conducted on 28/01/19 and the search on CINAHL, Web of Science grey literature databases was conducted on 16/02/19. This search strategy was conducted by a second reviewer to confirm that these searches could be replicated in each database and to resolve any large differences found in numbers of studies retrieved. They conducted the search on all databases on 16/09/19 apart from PsychINFO on 12/09/19 and the grey literature on 18/09/19. The same number of papers were retrieved using PsychINFO and the grey literature databases, whereas larger numbers of papers were retrieved from the remaining databases. These numbers ranged from an increase in 18 to 181 papers, which was to be expected due to the 7 to 8-month time gap between the first and second review.

2.2 Study Selection Process

Studies from the six databases were gathered in EndNote and duplicates were removed. After titles and abstracts were reviewed for relevance full-text papers were reviewed using the following criteria:

Inclusion Criteria

- Papers published between 1990 – 2019
- Quantitative studies
- Observational cohort and cross-sectional studies
- Studies published in English language
- Studies reporting original research in peer-reviewed journals
- HS diagnosed by physician
- Studies reporting HS data separately from other dermatological diseases (with sufficient sample detail)

Exclusion Criteria

- Interventional and qualitative studies
- Case studies
- Reviews, abstracts, communications, correspondence
- Studies focused on other health conditions
- HS data not reported separately from other conditions
- Mean age of subjects below 18 / focus on paediatric population
- Number of participants < 10
- Studies not focused on psychological outcomes
- Non-validated/unpublished measures of anxiety, depression and quality of life
- Studies without an overall/total score on a validated measure of quality of life / anxiety / depression

Historically severity of HS has been measured by clinicians using clinical/physical measures, however research has highlighted the importance of assessing both physical and psychological severity using validated self-reported measures (Pavon Blanco et al., 2018). This is also the case in another inflammatory skin disease (Kirby et al., 2001). In view of these findings and the importance of using validated measures for accuracy, studies that did not state an overall or total score of quality of life, anxiety or depression as measured by a validated self-reported questionnaire were excluded. This was due to this limiting the ability to draw overall conclusions about these areas and make clear comparison between studies that used different measures. A second independent reviewer (APB) assessed 20% of the full text articles screened and 22% of the final eligible studies

for whether they met the inclusion/exclusion criteria. These studies were selected by using the random generator function in Microsoft Excel.

2.3 Quality Assessment

The National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (Appendix C) was used to assess methodological quality of the papers (National Institutes of Health [NIH], 2014) and a second reviewer assessed all papers. Disagreements were resolved through discussion, and a third researcher was consulted if agreement was not reached. The NHLBI tool includes 14 questions to assess the quality of studies, with "yes / no" responses or "cannot determine / not applicable / not reported" depending on study characteristics. Question 8 of this tool refers to whether exposures that can vary in amount or level are examined at different levels of the exposure as related to the outcome (NIH, 2014); this question was answered based on whether HS duration and/or severity was assessed in relation to the outcomes. This tool allowed reviewers to rate the quality as "poor", "fair" or "good", and was selected as it has been used in numerous systematic reviews investigating prevalence of depression, anxiety and quality of life in physical health problems (Briggs, Kenny & Kennelly, 2016; Christensen, Ipsen, Doherty & Langberg, 2016; Ismail et al., 2017; Maass, Roorda, Berendsen, Verhaak & de Bock, 2015).

2.4 Data Extraction

Study characteristics were extracted from the eligible articles including author names, year of publication, journal, study design, sample type (including location of study), number of participants with HS, number of participants in comparison group(s) if applicable, mean age (standard deviation and range if available) and gender. Study findings included measures of outcomes and possible contributing factors, overall results of prevalence of quality of life / anxiety / depression, and factors that had significant effects on prevalence.

As a minimum requirement study designs and findings were looked at pragmatically despite how they had been labelled in the article. Four authors were contacted to request information that was not presented in their papers (including participant numbers, demographics and a total measure of quality of life). Their

permission was granted for these to be included in this review. Data extraction for quality of life was conducted and interpreted in line with how each paper measured and referred to quality of life.

2.5 Data Synthesis

The mean scores for quality of life were amalgamated in a graph in order to quantify the prevalence of poor quality of life in HS across the studies. The methodological quality of the studies was also included in this graph to take into account the robustness of their findings and where the true value may lie. It should be noted that this is not a meta-analysis, however this method of data synthesis was used in order to demonstrate an overall prevalence of quality of life in this review.

3. Results

3.1 Study Selection

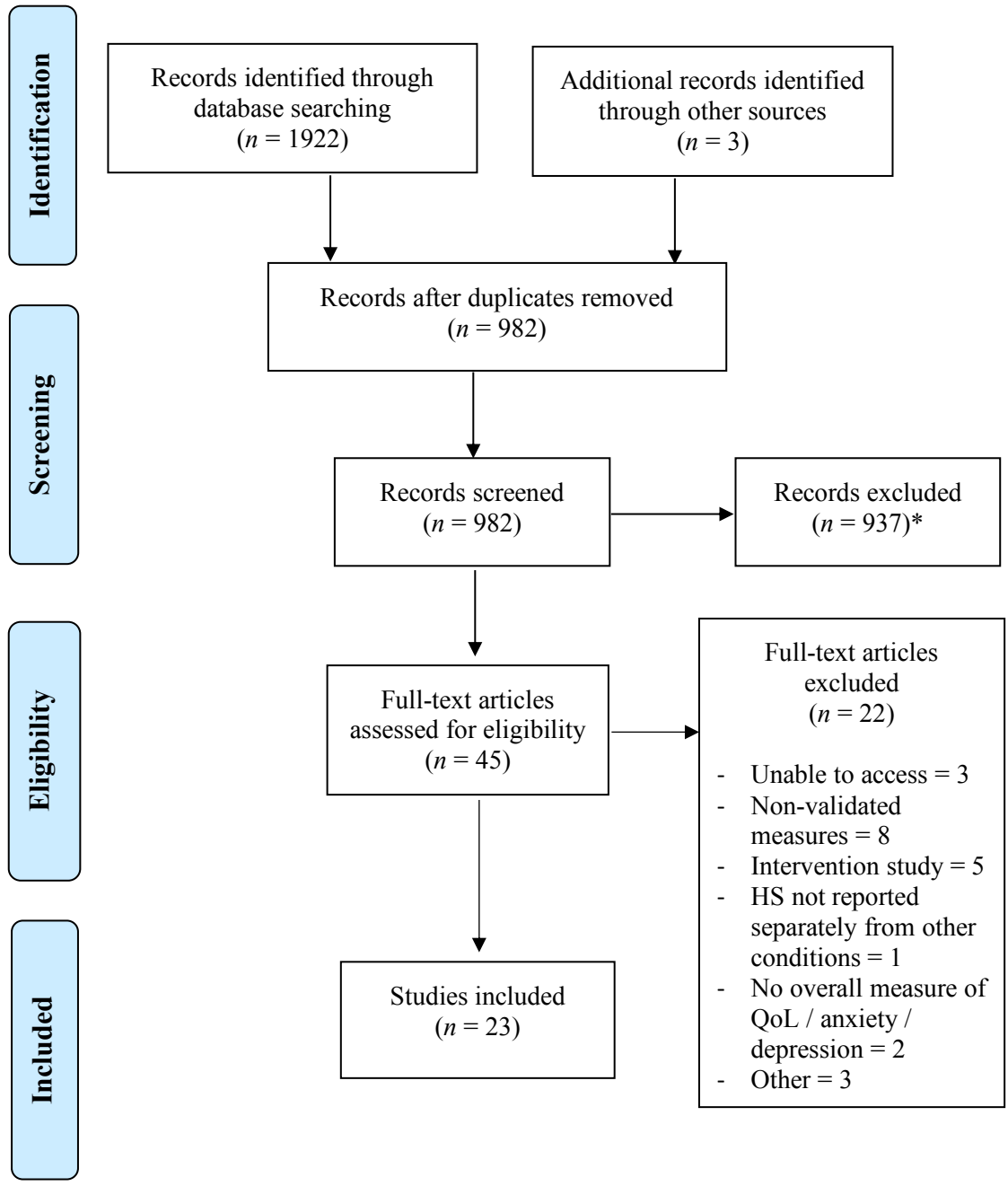
At the initial search stage 1925 were identified and 982 titles and abstracts were reviewed for relevance (studies with a focus on HS and psychological outcomes) following removal of duplicates. The most frequent reason for exclusion at this screening stage was that articles were not focused on psychological outcomes (n = 690), and the second most common reason was that the articles were either reviews, abstracts or correspondence (n = 128). There were 45 full texts that were evaluated for eligibility, and 23 of these papers were included in the review (Tables 1 and 2 include details of these papers). Figure 1 shows the numbers of papers reviewed and excluded at each stage and Appendix B shows the reasons for exclusion.

3.2 Overall Study Characteristics

All studies were cross-sectional (see Table 1) however not all studies stated their study design. Three papers reported being prospective studies, however when looked at in detail it was not evident why they had been labelled as prospective. One study stated that it was a case series, however the data reported was not in line with the criteria for a case series design.

Figure 1.

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Flowchart



Note. See Appendix B for details on reasons for exclusion.

All participants with HS were recruited either through hospitals or HS clinics apart from one study where participants were recruited from a national Blood Donor sample (Theut Riis et al., 2019). Seven studies included participants under the age of 18, however the mean ages of participants in these papers were over age 30. Overall, the mean age of participants with HS ranged from 32.5 – 45.95; the mean age fell within the thirties in 16 of the studies.

Twenty of the studies (87%) had a majority of female participants, with nine papers having more than double the number of females than males. Proportions ranged from 10% female and 90% male (Agut-Busquet, Romani, Ribera & Luelmo, 2019) to 86% female and 14% male (von der Werth & Jemec, 2001). Sample sizes of participants with HS ranged from 26 - 500 and overall samples ranged from 26 - 27765. Eleven of the studies (48%) had at least one comparison group; eight included healthy controls or the general population. Only four of these studies matched controls for age and sex (Alavi, Farzanfar, Rogalska, Lowes & Chavoshi, 2018b; Kaaz, Szepietowski & Matusiak, 2018) and age, body mass index (BMI) and sex (Kurek et al., 2012; Kurek et al., 2013). Five studies compared participants with HS with participants with other skin diseases. Two compared HS directly with psoriasis (Kluger, Sintonen, Ranta & Serlachius, 2018; Storer, Danesh, Sandhu, Pascoe & Kimball, 2018), whilst three used comparisons with cohorts that included various skin conditions (Balieva et al., 2017; Balieva et al., 2018; Onderdijk et al., 2013).

3.3 Measures Used to Assess Prevalence and Associated Factors

Table 2 outlines the tools used to measure anxiety, depression, quality of life and other factors that were assessed for associations.

3.3.1 Anxiety

Anxiety was assessed in three studies (Kouris et al., 2016; Kurek et al., 2013; Pavon Blanco et al., 2018). Measures of anxiety included the Generalised Anxiety Disorder 2-item (GAD-2; Kroenke, Spitzer, Williams, Monahan & Löwe, 2007) and the HADS (Zigmond & Snaith, 1983).

3.3.2 Depression

Depression was assessed in eight studies. Measures included the HADS in two studies (Kouris et al., 2016; Kurek et al., 2013), the Major Depression Inventory (MDI; Bech & Wermuth, 1998) in two studies (Onderdijk et al., 2013; Theut Riis et al., 2019), the Beck Depression Inventory-21 item (BDI-21; Beck et al., 1961) in another two studies (Kluger et al., 2017; Kluger et al., 2018), the BDI-Short Form (BDI-SF; Groth-Marnat, 1990) used in Matusiak et al. (2010), and finally the Patient Health Questionnaire-2 (PHQ2; Kroenke, Spitzer & Williams, 2003) used in Pavon Blanco et al. (2018).

3.3.3 Quality of Life

Quality of life was assessed in 21 of the studies. Measures included the DLQI (Finlay & Khan, 1994) in 19 studies (90%) and the Euro Quality Visual Analogue Scale (EQ-VAS; EuroQol Group, 1990) in two studies. A modified DLQI (six questions), the Skindex-29 (Chren et al., 1997), the Hidradenitis Suppurativa Impact Assessment (HSIA; Kimball et al., 2018), the Euro Quality of Life Health Outcome Measure (EQ5D; EuroQol Group, 1990), the Short Form 36 Version 2 health survey (SF-36v2; Ware Jr et al., 1995), the Short Form-12 (SF-12; Ware Jr, Kosinski & Keller, 1996), the 15D (Sintonen & Richardson, 1994) and a novel measure developed by the study investigators (Alavi et al., 2015) were included in one study each. The Time Trade-Off utility (TTO; Oppe, Rand-Hendriksen, Shah, Ramos-Goni & Luo, 2016) was also included in one study which measures years participants are willing to trade in return for skin disease-free living versus obesity.

3.3.4 Additional Factors

Disease severity was measured in 20 studies (87%), with several studies using multiple severity measures. Hurley staging (Hurley, 1989) was used in 17 studies, Sartorius Scores (Sartorius et al., 2003; Sartorius et al., 2009) in four studies, and the PGA scale (Kimball et al., 2012; Zouboulis et al.., 2015) in two studies. Other measures included Hidradenitis Suppurativa Index 4 (HSI4; Zouboulis et al., 2017), Hidradenitis Suppurativa Score (HSS; Sartorius et al., 2009), Hidradenitis Suppurativa Symptom Assessment (HSSA; Kimball et al., 2018), Hidradenitis Suppurativa Severity Index (HSSI; Grant, Gonzalez, Montgomery, Cardenas & Kerdel, 2010), International HS Severity Score System (IHS4; Zouboulis et al., 2017), and one study measured this using the average number of painful lesions.

Sexual functioning was measured in five studies, four of which used the International Index of Erectile Dysfunction (IIEF; Rosen et al., 1997) and the Female Sexual Function Index (FSFI; Rosen et al., 2000). The Sexual Quality of Life Questionnaire (SQoLM; Abraham et al., 2009), Female Sexual Distress Scale - Revised (FSDS-R; DeRogatis, Clayton, Lewis-D'Agostino, Wunderlich & Fu, 2008), Frankfurt Self-Concept Scale for Sexuality (FKKS SSEX, Deusinger, 1982) and the Arizona Sexual Experience Scale (ASEX; McGahuey et al., 2000) were also used amongst these studies.

Pain was measured using a Visual Analogue Scale (VAS; Jensen & Karoly, 2011) in two studies and a numeric rating scale (1-10) in another study. Sleep (Athens Insomnia Scale [AIS], Soldatos, Dikeos & Paparrigopoulos, 2000; Pittsburgh Sleep Quality Index [PSQI], Buysse, Reynolds, Monk, Berman & Kupfer, 1989) and fatigue (Functional Assessment of Chronic Illness Therapy - Fatigue Scale [FACIT-F], Cella, Lai, Cahng, Peterman & Slavin, 2002) factors were measured. Illness perceptions (Brief Illness Perception Questionnaire [BIPQ], Broadbent, Petrie, Main & Weinman, 2006), odour severity and frequency (Likert scales), workability (Work Productivity and Activity Impairment-Specific Health Problem [WPAI-SHP], Reilly, Zbrozek & Dukes, 1993), loneliness (UCLA Loneliness Scale Version 3, Russel, 1996), C-reactive protein (blood drawn), and stigmatization (Evers et al. [2001] "6-Item Scale") were also explored.

3.4 Methodological Quality of Eligible Studies

The overall quality ratings of the papers are included in Table 2 and the quality assessments for each paper are included in Appendix D. Three studies were rated as 'good' quality, 13 were rated as 'fair' and seven were rated as 'poor'. Quality issues that were found in these studies included lack of information on: method (two), participant age/gender/numbers (four), mean scores of outcome measures (two), whether potential confounding variables had been controlled for (nine), incorrect labelling of study design (three), small sample sizes (two), potential selection bias (four) and measurement bias (nine) and not clearly stating the research question / objectives (three).

3.5 Findings

3.5.1 Prevalence of Anxiety in HS

Three studies measured the prevalence of anxiety in HS participants. Pavon Blanco et al. (2018) found that the mean score on the GAD-2 across participants was below clinical threshold for anxiety, however 27% scored equal to or above threshold. The mean score for anxiety in the study by Kouris et al. (2016) also indicated that participants with HS were in the normal range. It should be noted that their anxiety scores were significantly higher than healthy controls, therefore experiencing more symptoms of anxiety than people without HS. Kurek et al. (2013) assessed anxiety as a contributing factor to prevalence of depression in participants with HS, however the mean score for anxiety was not reported in the paper.

3.5.2 Factors Associated with Anxiety

Participant beliefs about having HS were found to be a significant factor associated with levels of anxiety in Pavon Blanco et al.'s (2018) study. In particular, high emotional response, more negative perceived consequences and lower concern about HS were significantly related to higher anxiety. Illness beliefs also explained the greatest proportion of variance in anxiety over disease severity, which did not explain further variance than demographic variables. However, in the study by Kouris et al. (2016) greater disease severity (Hurley stage III) was found to be a significant factor associated with higher anxiety, compared to stages I and II which did not differ significantly. Depression was also positively correlated with anxiety in Kurek et al.'s (2013) study.

3.5.3 Prevalence of Depression in HS

Eight studies measured the prevalence of depression in HS participants, and all eight found that typically participants did not meet the threshold for clinical depression (two of these studies present the same data – Kluger et al., 2017; Kluger, et al., 2018). Four of the studies compared depression rates in HS with other groups (including healthy controls, people with psoriasis and other dermatological diseases), of which three found HS participants to score significantly higher on depression scores than the controls. The prevalence of participants meeting clinical threshold for depression was between 35 – 38.6% in four studies (Kluger et al., 2017; Kluger et al., 2018; Kurek et al., 2013;

Table 1.

Study Characteristics

Paper reference, journal	**Study design**	**Sample type (location)**	**Number with HS**	**Number in comparison group(s)**	**Mean age (*SD* / range if available)**	**Gender**
Agut-Busquet et al. (2018), Journal of Dermatology	Cross-sectional	People with HS in a hospital (Spain)	377 (Nape involvement: 30 & Non-nape: 347)	NA	Nape: 36.24, range: 23 - 66. Non-nape: 36.83, range: 10 - 79 (this was not available in the journal article therefore authors were contacted)	Nape: F: 10%. M: 90%. Non-nape: F: 45.4%. M: 54.6%
Alavi et al. (2015), American Journal of Clinical Dermatology	Case series (prospective)	Adults in HS community clinics (Canada)	55	NA	39 (range: 21 - 69)	F: 69%. M: 31%
Alavi, Farzanfar, Lee & Almutairi (2018a), Journal of Cutaneous Medicine and Surgery	Cross-sectional	Adults with HS in a hospital and community clinic (Canada)	51	NA	32.5 (*SD*: 10.76)	F: 71%. M: 29%
Alavi et al. (2018b), International Journal of Women's Dermatology	Cross-sectional	Adults with HS in a hospital and community clinic & healthy controls matched for age & sex (Canada)	50	50	HS: 35.98 (*SD*: 13.62). Control: 39.80 (*SD*: 11.80)	HS: F: 66%. M: 34%. Control: F: 56%. M: 44%.
Balieva et al. (2017), British Journal of Dermatology	Cross-sectional	Adults in dermatological outpatient clinics & healthy controls (workers without skin disease) (Europe)	48	Total participants with skin disease: 4010. Control: 1359	Total participants with skin disease: 47.1 (*SD*: 18.0). HS: 40.3 (*SD*: 12.2). Control: 41.1 (*SD*: 13.6)	Total participants with skin disease: F: 56.3%. M: 43.7%. HS: F: 79.2%. M: 20.8%.

						Control: F: 66.6%. M: 33.4%
*Balieva et al. (2018), Acta Dermato-Venereologica	Cross-sectional	Adults in dermatological outpatient clinics & controls (adults with naevi) (Europe)	48	Total participants with skin disease: 4010. Control: 1359	Total participants with skin disease: 47.1 (*SD*: 18.0). HS: 40.3 (*SD*: 12.2). Control: 41.1 (*SD*: 13.6) (this was not available in the journal article therefore authors were contacted)	Total participants with skin disease: F: 56.3%. M: 43.7%. HS: F: 79.2%. M: 20.8%. Control: F: 66.6%. M: 33.4% (this was not available in the journal article therefore authors were contacted)
Calao et al. (2018), PLOS ONE	Cross-sectional	Adults in HS clinics (Australia)	117	NA	39.4 (*SD*: 13.8, range: 18.1 - 71.8)	F: 66.7%. M: 33.3%
Janse et al. (2017), British Journal of Dermatology	Cross-sectional	Adults with HS in dermatological clinics and a hospital (Holland)	300	NA	44.6 (*SD*: 12.1) – calculated from gender numbers presented in the paper.	F: 78%. M: 22%
Kaaz et al. (2018), Acta Dermato-Venereologica	Cross-sectional	People with HS in a hospital & age/sex-matched healthy controls (Poland)	108	50	HS: 36.3 (*SD*: 12.1, range: 15 - 67). Control: 40.4 (*SD*: 9.1, range: 23 - 57)	HS: F: 47%. M: 53%. Control: F: 50%. M: 50%
Katoulis et al. (2017), Skin Appendage Disorders	Cross-sectional (prospective)	People with HS in a hospital (Greece)	152	NA	37.4 (*SD*: 13.5, median: 37, range: 13 - 96)	F: 60.5%. M: 39.5%
Kluger, Ranta & Serlachius (2017), Skin Appendage Disorders	Cross-sectional	Adults with HS in a hospital (Finland)	26	NA	44.2 (*SD*: 15.5)	F: 61.5%. M: 38.5%

*Kluger et al. (2018), Skin Appendage Disorders	Cross-sectional	Adults with HS, age standardised general population & people with psoriasis from Health Examination Survey (Finland)	26	General population: 4176. Participants with psoriasis: 138	HS: 44.2 (*SD*: 15.5)	F: 61.5%. M: 38.5%
Kouris et al. (2016), Dermatology	Cross-sectional	People with HS & healthy controls (Greece)	94	94	HS: 34.55 (*SD*: 10.30). Controls: 34.96 (*SD*: 10.42)	HS: F: 54%. M: 46%. Control: F: 53%. M: 47%
Kurek et al. (2012), The American Academy of Dermatology	Cross-sectional (prospective case-control)	Adults with HS in a hospital & age/sex/BMI-matched healthy controls - matched pairs (Germany)	44	41	HS: 34.3 (*SD*: 10.7, range 18 - 59). Control: 37.1 (*SD*: 11.0, range: 10 - 59)	HS: F: 55%. M: 45%. Control: F: 51%. M: 49%
*Kurek et al. (2013), Journal of the German Society of Dermatology	Cross-sectional (case-control)	Adults with HS in a hospital & age/sex/BMI-matched healthy controls - matched pairs (Germany)	44	41	HS: 34.3 (*SD*: 10.7, range 18 - 59). Control: 37.1 (*SD*: 11.0, range: 10 - 59)	HS: F: 55%. M: 45%. Control: F: 51%. M: 49%
Matusiak et al. (2010), Acta Dermato-Venereologica	Cross-sectional	People with HS in a hospital (Poland)	54	NA	39.94 (*SD*: 11.63, range: 16 - 65)	F: 52%. M: 48%
Onderdijk et al. (2013), Journal of the European Academy of Dermatology and Venereology	Cross-sectional	People with HS in 2 hospitals & other dermatological outpatients as controls (Denmark & the Netherlands)	211	233	HS: 43 (*SD*: 11.8, range: 16 - 70). Control: 42 (*SD*: 13.5, range: 9 - 77)	F: 77%. M: 23%
Pavon Blanco et al. (2018), British Journal of Dermatology	Cross-sectional	Adults in a HS tertiary clinic (England)	211	NA	38.2 (*SD*: 11.8, range: 17 - 71)	F: 60%. M: 40%

Rondags et al. (2019), British Journal of Dermatology	Cross-sectional	Adults with HS from 2 tertiary referral centres (Netherlands)	433	NA	39 (*SD*: 12.4)	F: 72.3%. M: 27.7%
Sartorius et al. (2009), British Journal of Dermatology	Cross-sectional	People with HS in specialist centre (Sweden)	251 (246 completed DLQI)	NA	37.5 (*SD*: 11.4, range: 14 - 67)	F: 86%. M: 14%
Storer et al. (2018), International Journal of Women's Dermatology	Cross-sectional	Adults with HS and adults with psoriasis in a hospital (US)	32	47	HS: 34 (*SD*: 11). psoriasis: 51 (*SD*: 16)	HS: F: 72%. M: 28%. psoriasis: F: 45%. M: 55%
Theut Riis et al. (2019), British Journal of Dermatology	Cross-sectional	People with HS participating in nationwide Danish Blood Donor Study (Denmark)	500	27265	HS: 36.57 (*SD*: 11.32). None-HS: 41.30 (*SD*: 12.80)	HS: F: 49.8%. M: 50.2%. Non-HS: F: 45.7%. M: 54.3%
von der Werth & Jemec (2001), British Journal of Dermatology	Cross-sectional	Adult with HS in 4 hospitals (UK & Denmark)	114	NA	40.9 (*SD*: 11.7, range: 20 - 76)	F: 86%. M: 14%

*Same study cohort as previous study with different measures reported.

Table 2.

Study Findings

Paper reference	Measures	Main findings	Factors significantly impacting findings	Quality rating
Agut-Busquet, Romani, Ribera & Luelmo (2018)	Disease severity: Hurley staging, Sartorius Score, Hidradenitis Suppurativa Index 4 (HSI4), Physician Global Assessment (PGA) scale. QoL: Dermatology Quality of Life Index (DLQI)	Nape: very large impact on QoL (Mean DLQI: 14.53 ± 7.17). Non-nape: moderate impact on QoL (Mean DLQI: 10.72 ± 7.18). Overall DLQI mean: 11.02 ± 7.18 (not available in journal article - this was calculated from the two sample means).	Nape involvement	Fair
Alavi, Anooshirvani, Kim, Coutts & Sibbald (2015)	Disease severity: Hurley staging. QoL: DLQI, Short Form 36 Version 2 (SF-36v2) health survey (physical and mental component scores), and a questionnaire designed by investigators (age, time to diagnosis, duration of first symptom, no. of lesions, no. of episodes, QoL (mild, moderate, severe). Sexual functioning: IIEF, FSFI, FSDS-R.	Moderate impact on QoL. Mean DLQI: 10 ± 8.8. SF-36v2 scores: significantly lower than normal. PCS: 45 ± 10.6. MCS: 47 ± 11.5.	Disease severity, number of lesions	Fair
Alavi et al. (2018a)	Disease severity: Hurley staging, Sartorius System, PGA. QoL: DLQI, Skindex-29. Odour severity/frequency: Likert scales (0 - 10 & 0 - 4).	Mean DLQI: very large impact (15.10 ± 1.64). Mean Skindex-29: severe impact (65.33 ± 17.80)	Odour severity (on Skindex-29), gender (on DLQI)	Fair
Alavi et al. (2018b)	Disease severity: Hurley staging. QoL: DLQI. Sexual functioning: Sexual Quality of Life Questionnaire (SQoLM), International Index of Erectile Dysfunction (IIEF), Female Sexual Function Index (FSFI), Female Sexual Distress Scale - Revised (FSDS-R).	Very large impact on QoL. Mean DLQI: 17.63 ± 6.62 (unclear in journal article therefore authors were contacted). Mean DLQI completed by 46 controls: 4.98 ± 5.59 (this was not available in the journal article therefore authors were contacted).	Disease severity, sexual functioning, number of lesions	Fair

		Significantly lower QoL than controls ($p < .0001$)		
Balieva et al. (2017)	QoL: Euro Quality Visual Analogue Scale (EQ-VAS: 0 - 100, worst-best health state), Euro Quality of Life Health Outcome Measure (EQ5D: -0.594 – 1 (full health))	HS had severely reduced HRQoL - lowest self-reported health (Mean EQ-VAS: 56.9 ± 20.7). Significantly lower than controls (Mean EQ-VAS: 82.2 ± 15.5). Mean EQ-VAS of total participants with skin disease: 69.9 ± 19.7.	NR	Fair
Balieva et al. (2018)	QoL: DLQI	Very large impact on QoL: Mean DLQI: 12.7 ± 7.6 for 46 HS participants. Mean DLQI of total participants with skin disease: 6.7 ± 6.8 (moderately impaired). Mean DLQI for naevi (controls): 1.52 ± 2.9 (no impact)	NR	Fair
Calao et al. (2018)	Disease severity: Hurley staging. QoL: DLQI.	Very large effect on QoL. Mean DLQI: 11.8 ± 8.1. 49.6% had a very large or extremely large impact on QoL.	NR	Fair
Janse et al. (2017)	Disease severity: Hurley staging, PGA, pain score on VAS. QoL: DLQI. Sexual Health: FSFI, IIEF, Arizona Sexual Experience Scale (ASEX).	Very large effect on QoL. Mean DLQI: 12.5 ± 7.5.	Disease severity and activity, pain, sexual functioning in women, anogenital involvement, early onset of HS	Poor
Kaaz et al. (2018)	Disease severity: Hidradenitis Suppurativa Score (HSS), Hidradenitis Suppurativa Severity Index (HSSI), Hurley staging. QoL: DLQI. Pain: VAS (current & most intense experienced). Sleep: Athens Insomnia Scale (AIS), Pittsburgh Sleep Quality Index (PSQI).	Very large effect on QoL. Mean DLQI: 13.0 ± 8.0. DLQI score for controls not available.	Sleep quality	Fair
Katoulis et al. (2017)	Disease severity: Hurley staging. QoL: DLQI.	Very large effect on QoL. Mean DLQI: 11.9 ± 7.7.	Disease severity	Fair

Kluger et al. (2017)	Disease severity: Hurley staging, Hidradenitis Suppurativa Symptom Assessment (HSSA). Depression: Beck Depression Inventory-21 item (BDI-21). QoL: DLQI, Hidradenitis Suppurativa Impact Assessment (HSIA). Impact on workability: Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP)	Moderate effect on QoL: Mean DLQI: 8.31. Mean BDI-21 score: 10.69 ± 10.13 (normal range). 38.5% met clinical threshold.	Disease severity, gender, BDI score.	Good
Kluger et al. (2018)	Disease severity: Hurley staging. QoL: DLQI, The 15D. Depression: BDI-21.	Moderate effect on QoL: Mean DLQI: 8.31 ± 7.39. No comparison group data. Mean 15D: 0.882 ± 0.083 (clinically important). Statistically and clinically significantly lower than general population (0.935 ± 0.071). Lower than participants with psoriasis: 0.900 ± 0.117 (non-significant difference). Mean BDI-21: 10.69 ± 10.13 (normal range). No comparison group data.	Gender, depression and DLQI score.	Fair
Kouris et al. (2016)	Disease severity: Hurley staging. QoL: DLQI. Anxiety & Depression: The Hospital Anxiety and Depression Scale (HADS). Loneliness: UCLA Loneliness Scale (Version 3).	Very large effect on QoL: Mean DLQI: 11.43 ± 6.61. No DQLI score for controls. Anxiety in normal range: Mean HADS: 6.41 ± 3.31. Controls: 5.00 ±1.59. Depression in normal range: Mean HADS: 5.45 ± 2.79. Controls: 4.16 ± 1.54. Statistically significantly higher anxiety and depression than controls.	QoL: gender, loneliness, depression, anxiety Depression and anxiety: disease severity	Poor
Kurek et al. (2012)	Disease severity: Sartorius Score. QoL: DLQI. Sexual function: FSFI, Frankfurt	Very large effect on QoL Mean DLQI: 12.2 ± 7.0. No DQLI score for controls.	Sexual functioning (for females), gender, disease severity	Fair

	Self-Concept Scale for Sexuality (FKKS SSEX), IIEF.			
Kurek et al. (2013)	Disease severity: Sartorius score. Sexual function: FKKS SSEX. Anxiety and depression: HADS. C-reactive protein: blood drawn.	Depression in normal range: Mean HADS: 6.4 ± 0.6. Statistically significantly higher than controls (2.6 ± 0.4). About 38.6 % (*n* = 17) met threshold for depression (compared to 2.4 %, *n* = 1 of controls)	Disease severity, anxiety, sexual distress, C-reactive protein levels	Good
Matusiak et al. (2010)	Disease severity: Hurley staging. QoL: DLQI (also using Global Question indexing), Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF, 0 - 100%), EQ-5D, EQ-VAS. Depression: BDI Short Form (BDI-SF). Fatigue: Functional Assessment of Chronic Illness Therapy - Fatigue Scale (FACIT-F). Stigmatization level: Evers et al. "6-Item Scale".	Very large effect on QoL: Mean DLQI: 12.67 ± 7.7. EQ-5D: 0.66 ± 0.23. EQ-VAS: 56.78 ± 18.84. Q-LES-Q-SF: 56.44 ± 15.17% Depression in normal range. Mean BDI-SF: 5.87 ± 4.68. 21% of results suggested co-existence of depression (BDI ≥ 10).	QoL: location and no. of lesions, fatigue, disease severity, stigmatization level, age of onset Depression: age of onset, location of lesions, disease severity	Poor
Onderdijk et al. (2013)	Disease severity: Hurley staging. QoL: DLQI. Depression: Major Depression Inventory (MDI): depression rating scale/MDI score (≥ 20 indicates depression) and diagnostic score. Pain & itch: Numeric Rating Scales (0 - 10).	Moderate effect on QoL: Mean DLQI: 8.4 ± 7.5. Statistically significantly higher than participants with other dermatological conditions (4.3 ± 5.6). Mean MDI: 11.0 (significantly higher than participants with other dermatological conditions: 7.2). Clinically defined depression rate: 9% (*n* = 19) - not significantly higher than participants with other dermatological conditions (6%).	MDI score (not diagnostic score) for HS & controls: days with lesions in past month, pain, itch, sick-days due to skin disease in last 3 months, Hurley classification (HS only), number of flares in past month (HS only) QoL for HS & controls: MDI score, pain, itchiness, sick-days in last 3 months, number of flares in past month (HS only), Hurley classification (HS only)	Fair

Pavon Blanco et al. (2018)	Disease severity: Hurley staging. Depression: Patient Health Questionnaire-2 (PHQ-2). Anxiety: Generalised Anxiety Disorder 2-item (GAD-2). QoL: DLQI. Illness Perceptions: Brief Illness Perception Questionnaire (BIPQ).	Very large effect on QoL. Mean DLQI: 14.81 ± 8.45. Mean anxiety and depression scores below clinical threshold. GAD-2: 1.88 ± 1.86, 27% met threshold. PHQ-2: 2.12 ± 1.88, 35% met threshold.	Illness perceptions, disease severity	Good
Rondags et al. (2019)	Disease severity: Hurley staging, International HS Severity Score System. QoL: DLQI.	Moderate effect on QoL: Mean DLQI: 10.0 (5.0-16.0). No *SD* available.	Disease severity	Poor
Sartorius et al. (2009)	Disease severity: Hurley staging, VAS (pain) and additional clinical details to give an overall HS score. QoL: DLQI.	Moderate effect on QoL: Mean DLQI: 10.3 ± 7.5.	Disease severity	Poor
Storer et al. (2018)*	Disease severity: Hurley staging, psoriasis Area Severity index (PASI). QoL: Time Trade-Off (TTO) utility - years willing to trade in return for skin disease-free living versus obesity, DLQI (modified 6-question version).	Participants with HS who are obese significantly poorer QoL than participants with psoriasis who are obese in social interactions, clothing choice, leisure activities, ability to work/study. Skin disease had greater impact on QoL than obesity. TTO: HS more distressed and willing to trade significantly more years of life (7.4 / 20 year & 16 / 50 years) than those with psoriasis (3.2 years & 9.1 / 50 years).	Obesity	Poor
Theut Riis et al. (2019)**	Depression: MDI. QoL: Short Form-12 (SF-12: physical and mental component scores).	MDI: Significantly less HS in no depression range (94.5%) than non-HS (97.4%). Significantly more HS in moderate depression range (3.2%) than non-HS (0.7%). HS increased MDI by average of 1.427.	NR	Fair

		SF-12: No significant difference in PCS and MCS medians between groups (HS: 56.56 7 54.96, non-HS: 56.58 & 55.51). No significant effect of HS on PCS and MCS after adjusting for sex, age, BMI and smoking.		
von der Werth & Jemec (2001)***	Disease severity: average no. of painful lesions. QoL: DLQI	Moderate effect on QoL: Mean DLQI: 8.9 ± 8.3.	Age at onset, number of lesions per month	Poor

* A modified version of the DLQI was used (not a validated measure).

** HS was not formally diagnosed by a clinician in the study - a measure was used that was developed and validated by HS physicians (Vinding et al., 2013)

*** Disease severity was assessed by participants counting the number of lesions (not a validated measure of HS severity)

Pavon Blanco et al., 2018), 21% in Matusiak et al.'s (2010) study, 9% in Onderdijk et al.'s (2013) study and 5.5% in the study by Theut Riis et al. (2019). In Onderdijk et al.'s (2013) study mean MDI scores were significantly higher for HS than other skin disorders, however the number of people with HS who met clinical threshold was not significantly higher than other skin diseases. Theut Riis et al. (2019) found that there were significantly more people with HS in the moderate depression range than the non-HS group and significantly less in the no depression range. In the studies by Kluger et al. (2017) and Kluger et al. (2018) six people with HS were in the mild depression range, two were in the moderate range and two were in the severe range.

3.5.4 Factors Associated with Depression

Disease severity was found to be a factor significantly associated with higher levels of depression in four of the studies. In three of these studies this was measured using Hurley staging and the other used Sartorius scoring. Pavon Blanco et al. (2018) found that Hurley staging accounted for a higher amount of variance in depressive symptoms than demographic variables, and Kouris et al. (2016) found that people with Hurley Stage III experienced higher levels of depression than people at stage I and II (no significant difference between these two stages). Onderdijk et al. (2013) also found that Hurley classification positively correlated with depression scores, in addition to the number of flares in the last month. They also indicated that both people with HS and other dermatological diseases scored higher on depression measures when experiencing itch, more days with lesions in the past month, sick-days and pain due to their condition in the past 3 months (Onderdijk et al., 2013). In contrast to these findings, Kluger et al. (2017) and Kluger et al. (2018) reported that Hurley staging, the number of areas affected by HS and duration of HS were not significantly correlated with depression. Kurek et al. (2013) also found HS duration to be non-significantly associated with the degree of depression.

Pavon Blanco et al. (2018) reported that although disease severity explained a significant amount of variance in depression scores, illness beliefs explained a greater amount of variance than disease severity. Specifically, these beliefs related to HS being associated with severe consequences and lower treatment control.

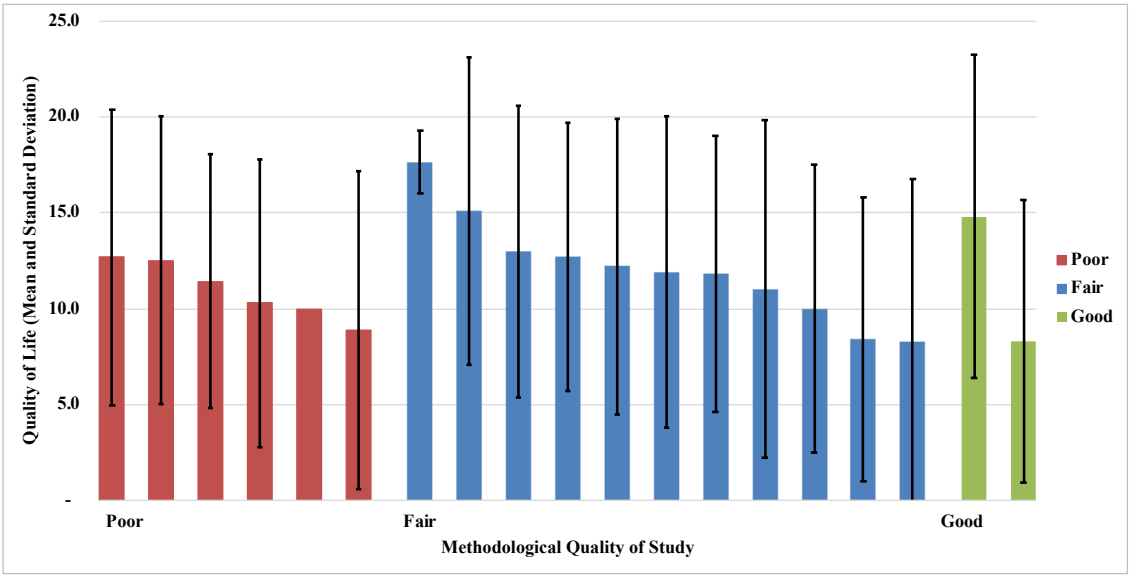
Female gender was found to be significantly associated with higher depression scores in the studies by Kluger et al. (2017) and Kluger et al. (2018), with 90% of the HS participants who met clinical threshold for depression being women. However, Kouris et al. (2016) found gender not to be significantly correlated. Other factors that were found to be significantly related to depression included later age of onset, poorer quality of life, higher anxiety, more sexual distress and higher C-reactive-protein levels. Age, age at HS diagnosis, comorbidities and number of comorbidities were not significantly related with depression.

3.5.5 Prevalence of Poor Quality of Life in HS

Twenty-two studies measured quality of life in people with HS, and in 19 of these the Dermatology Quality of Life Index (DLQI) was used to assess this. Seven of these studies found that the mean DLQI for people with HS was between 6 - 10 indicating that HS had a moderate impact on participant's quality of life. The remaining 12 studies found that the mean DLQI scores fell within 11 - 20 indicating that HS had a very large effect on the participants' lives. Figure 2 displays the 19 DLQI mean scores in relation to their methodological quality rating, in order to establish where the true value of quality of life in HS may lie. Kluger et al.'s (2018) mean DLQI is also displayed despite this being replicated from their previous study as both studies have different quality ratings. An overall mean DLQI score was calculated from the mean DLQI scores of both HS groups in Agut-Busquet et al.'s (2018) study as this was not available in the published article. The bar chart indicates that the majority of the fair quality studies found that HS typically had a very large impact on quality of life, which was also reflected in the poor quality studies. The two studies rated as good in methodological quality were split between moderate and a very large impact on quality of life. The consistency across varying study quality suggests that the true value of the impact of HS on quality of life is very large. It is also evident that the standard deviations were relatively large across 16 of the studies (this information was not available for one study), indicating the variability in the quality of life ratings within the samples. This variability may impact generalisability of the mean scores, however it may also indicate a true reflection of the wide-ranging impact of HS on quality of life, as opposed to study quality.

Figure 2.

Bar Chart of Mean DLQI Scores and Standard Deviations Across 19 Study Cohorts and Their Quality Assessment Ratings



Alavi et al. (2018b) used the DLQI and the Skindex-29; the Skindex-29 indicated a severe impact of HS on quality of life (the highest category) whereas the DLQI indicated a very large impact (the maximum DLQI range is 'extremely large impact'). The EQ-5D & EQ-VAS were used in two studies (Balieva et al., 2017; Matusiak et al., 2010). The EQ-VAS uses a 0 - 100 scale for worst-best health state, and in each study the mean rating for participants with HS was 56.9 and 56.78. The EQ-5D is rated from -0.594 (worst QoL) to 1 (full health), and in Matusiak et al.'s (2010) study the mean score was 0.66. A total index was not calculated in Balieva et al.'s (2017) study however it was found that the HS group was highest in the pain/discomfort category and had a five- and six-fold increased risk of impaired self-care and mobility / engaging in usual activities respectively. The Q-LES-Q-SF (Endicott, Nee, Harrison & Blumenthal, 1993) was also used in this study which is reported as a percentage with higher percentages indicating greater enjoyment and satisfaction. The overall percentage in quality of life was 56.44. The SF-36V1 was used by Alavi et al. (2015) and indicated that people with HS were scoring significantly lower than normal on mental and physical health indexes, specifically in areas of general health, pain, social functioning and the impact of emotional difficulties on the quality of activities such as work and time taken to complete tasks.

Four studies compared HS participants to healthy controls. Two of these studies (Alavi et al. 2018b; Balieva et al., 2018) that used the DLQI found that participants with HS had significantly poorer quality of life (very large impact) than healthy controls (small and no impact). Moreover, Balieva et al. (2017) used the EQ-VAS and found that the HS group reported significantly lower quality of life than healthy controls. Theut Riis et al. (2019) used the SF-12 and found that although HS participants rated their mental health as lower than the healthy controls there was no overall significant difference in quality of life between the two groups. Overall, three out of four studies found people with HS to have poorer quality of life than healthy participants. One study (Kluger et al. 2018) compared HS to the general population. This study used the 15D to measure quality of life which provides an overall score of health-related quality of life on a scale of 0 (dead) – 1 (full health). HS participants' quality of life was in the clinical range (0.882), and was also found to be significantly poorer than that in the general population (0.935).

Five studies compared HS to other dermatological diseases. Three studies found that people with HS had poorer quality of life scores, compared to participants with other skin diseases (Balieva et al., 2017; Balieva et al., 2018; Onderdijk et al., 2013). Balieva et al. (2017) reported HS as scoring the lowest self-reported health out of all the skin diseases measured and the third lowest on the EQ-VAS. Two studies compared HS directly with psoriasis (Kluger et al., 2017; Storer et al., 2018). Kluger et al. (2018) found that people with HS scored lower (0.882) than the participants with psoriasis (0.900) on the 15D, however this difference was not statistically significant. Storer et al. (2018) used Time Trade Off and a modified 6-item version of the DLQI (not a validated measure). They found that people with HS were more distressed and willing to trade significantly more years of life (7.4 / 20 year & 16 / 50 years) than those with psoriasis (3.2 years & 9.1 / 50 years). They also found that obese participants with HS scored significantly poorer on items of social interaction, clothing choice, leisure activities and ability to work/study than obese participants with psoriasis that were of a similar BMI. Overall, people with HS had poorer quality of life than people with other skin diseases in all five studies measuring this.

3.5.6 Factors Associated with Poor Quality of Life

Factors associated with quality of life were measured in 18 studies.

Demographics Factors

Gender was found to be a significant factor associated with quality of life in five studies, with females reporting poorer quality of life than males on the DLQI. In the majority of these studies the mean DLQI for males fell within the moderate range whereas females fell within the very large to extremely large impact range. In Kluger et al.'s (2017) study the mean DLQI for males indicated a small effect on quality of life in contrast to females who reported a very large impact on quality of life. Despite these findings Alavi et al. (2018a) found that gender was associated with quality of life as measured by the DLQI but found no difference in gender when using the Skindex-29. Three other studies also reported no significant correlation between gender and quality of life.

Four studies looked at age of participants in relation to quality of life and did not find a significant association (Alavi et al., 2015; Kluger et al., 2017; Kurek et al., 2012; von der Werth & Jemec, 2001). Matusiak et al. (2010) found no significant association of quality of life with level of education, place of residence and employment status, and Janse et al. (2017) found no association with relationship status.

Psychosocial and Lifestyle Characteristics

Psychosocial and lifestyle characteristics were significantly associated with quality of life in eight studies. The quality of life of participants with more negative beliefs about their HS was significantly more impaired than those with less negative beliefs about HS in Pavon Blanco et al.'s (2018) study. These illness perceptions also explained a greater proportion of variance in quality of life than the severity of their disease. Depression (four studies) and anxiety (one study) were significant factors associated with poorer quality of life in people with HS. Higher scores of loneliness (Kouris et al., 2016) and poor sleep (Kaaz et al., 2018) were also associated with poorer quality of life.

Difficulties with sexual functioning were assessed in three studies, and the majority of findings indicated a significant association with poorer quality of life. These associations were either only in females, or higher in females than males. Alavi et al. (2018b), Kurek et al. (2012) and Janse et al. (2017) found a significant correlation

between female sexual distress and dysfunction with poorer quality of life on four different measures of sexual function. In Janse et al.'s study (2017) this correlation also remained significant after removing the sexual health question from the DLQI. Alavi et al. (2018b) found that female and male sexual dysfunction and distress accounted for over 46% and 42% variance, respectively, in changes in quality of life after controlling for disease severity and number of lesions. No significant correlation was found between sexual functioning with quality of life for males.

Smoking (Kluger et al., 2017; Sartorius et al., 2009), BMI (Sartorius et al., 2009) and alcohol consumption (Kluger et al., 2017) did not significantly relate to quality of life in three studies. A study by Storer et al. (2018) found that obesity was outweighed by the psychological burden of HS in relation to impact on quality of life. The only category where HS participants reported significantly poorer quality of life than psoriasis participants was clothing choice. Obesity and other comorbidities including diabetes type II, cardiovascular diseases, anxiety disorders, autoimmune and inflammatory diseases were not associated with quality of life in HS (Kluger et al., 2018).

Clinical Characteristics of HS

In terms of disease severity, higher Hurley staging was significantly associated with poorer quality of life in 10 out of 11 studies that used this tool. Higher Sartorius Scores were a significant factor of impaired quality of life in one out of two studies, and PGA was only used in one study and was also a significant factor. Findings by Matusiak et al. (2010) indicated that Hurley staging was the most important factor associated with quality of life impairment, whereas Pavon Blanco et al. (2018) found that although Hurley staging added a significant amount of variance in quality of life beyond demographics, illness perceptions explained a larger proportion.

The number of lesions (measured in three studies) and number of lesions per month (measured in one other study) were significant factors associated with poorer quality of life in HS. However, location of lesions in two studies, and number of locations in one study were not significantly associated with quality of life. In terms of specific locations Alavi et al. (2018b) found that having genital lesions was not correlated with DLQI score, however participants with lesions in their nape area reported significantly higher quality of life impairment than those without nape involvement (Agut-Busquet et

al. 2018). Age at onset of HS was also investigated and found to be negatively correlated with quality of life in two studies, indicating that later age at onset was associated with poorer quality of life. A further two studies found that age of onset was not a significant factor associated with quality of life.

Pain was measured in two studies and findings indicated that it was significantly associated with poorer quality of life in HS. Itchiness, number of flares in the past month, number of sick days in the past three months (Onderdijk et al., 2013), disease activity (Janse et al. 2017) and odour severity (Alavi et al., 2018a) were also significant factors relating to poorer quality of life. It should be noted that Alavi et al. (2018a) found a non-significant association of odour severity on quality of life when using the DLQI as opposed to the Skindex-29, and Alavi et al. (2018b) also found that odour severity was not a predictor of DLQI in a regression model. Other factors that were analysed and found to be non-significant were the number of HS episodes, time until diagnosis, duration of first symptom (Alavi et al., 2015), region at onset (Kurek et al., 2012), and five studies measuring duration of disease.

4. Discussion

The aim of this review was to systematically explore existing research regarding the prevalence of anxiety, depression and poor quality of life in HS and factors associated with this. It is hoped that this will inform future research and provide implications for clinical practice in HS.

4.1 Prevalence of Anxiety and Associated Factors in People with HS

The literature that explored anxiety in HS and met the inclusion criteria was limited (three studies), as also found in Machado et al.'s (2019) systematic review. Overall, people with HS did not typically meet threshold for clinical or clinically significant anxiety (Kouris et al., 2016; Pavon Blanco et al., 2018), although a 27% prevalence rate was found in Pavon Blanco et al.'s (2018) study, which is higher than other recent research (Huilaja et al., 2018; Machado et al., 2019). Anxiety symptoms were more prevalent than healthy controls in Kouris et al.'s (2016) study, however this study was rated as methodologically poor due to insufficient information provided about the

recruitment process and analysis. It was therefore not possible to determine risk of bias. The findings from these two studies are in line with research by Machado et al. (2019) and Huilaja et al. (2018) that indicated higher prevalence rates than the global population in 2015 (WHO, 2017) and healthy controls, however Pavon Blanco et al. (2018) demonstrated a substantially larger prevalence rate. Kurek et al. (2013) did not include the HADS score for anxiety in their article, only the correlation with other factors, therefore it was not possible to establish a clear prevalence rate.

Factors that were associated with higher anxiety within these studies were symptoms of depression, more negative illness beliefs about HS, and HS severity being at Hurley stage III. The appearance (scarring and abscesses) and malodour of HS can negatively impact on body image, which may promote worry about others may perceive symptoms and attempts to hide them. This may explain findings that high disease severity was a factor in anxiety, as more areas of HS and stronger symptoms would make this more difficult for people to conceal. Shavit et al. (2015) also reported that increasing risk of accidentally exposing scars or odours relating to HS can contribute to anxiety. The severity of these symptoms and fear around how they may be perceived can also lead to more sick days (Alikhan et al., 2009), consequentially creating financial strains (Deckers & Kimball, 2016), thus contributing further to levels of anxiety.

Pavon Blanco et al. (2018) also demonstrated that negative illness perceptions about HS were more strongly associated with anxiety than disease severity. People who had a higher emotional response and more beliefs about negative consequences of HS had higher levels of anxiety independent of how severe their illness was. This is important to consider as it highlights that a clinical measure of HS by medical staff may not be representative of how patients see their illness and the impact it has on their mental health. Research into other skin diseases has discussed similar findings; Jowett and Ryan (1985) suggested that even when disease in is in remission, unpredictability of symptoms and prognosis are strong factors in the development of anxiety.

It is difficult to draw conclusions about the prevalence of anxiety in HS from this review due to the limited research available, however it is clear that negative beliefs about HS, disease severity and depression are factors to consider in relation to anxiety.

4.2 Prevalence of Depression and Associated Factors in People with HS

Depression in HS was another area that was limited in the literature (eight studies). Overall, participants with HS did not typically meet clinical thresholds for depression across these studies; in six of these articles prevalence of clinical depression rates ranged from 5.5% to 38.6%. Four of these studies had prevalence rates over 35%. This is higher than the overall prevalence found by Machado et al. (2019). Three out of four studies also found that people with HS had higher depression scores than healthy controls. Overall, prevalence rates that were reported indicated a maximum of 38.6% prevalence of depression which was higher than the prevalence of anxiety, and people with HS experienced significantly more symptoms of depression than healthy controls. This prevalence rate is in line with previous research by WHO (2017) and Lim et al. (2019) demonstrating the prevalence of depression in the general population as 4.4% and 12.9% respectively. Although prevalence of depression in HS was higher than in other dermatological diseases, this difference was not significant.

There were various factors that were associated with prevalence of depression in participants with HS. In line with factors associated with anxiety, negative illness beliefs about HS (specifically about HS having adverse consequences) was a factor, and higher disease severity was associated with depression in 50% of the studies. Other factors associated with higher scores of depression were pain, itch, the number of flares and lesions inthe last month, the number of sick-days due to HS in the last three months, later age of HS onset, poorer quality of life, sexual distress, c-reactive protein levels and female gender. Depression being more common in females with HS supports research by WHO (2017) and Shavit et al. (2015). Kouris et al. (2016) found that female gender did not significantly impact depression rates, however as stated previously, this study was rated as poor methodologically and therefore it could not be determined how this sample was recruited and if this impacted findings.

The numerous factors that were related to depression rates in people with HS (some of which overlapped with factors associated with anxiety) may link to Esmann and Jemec's (2011) findings of feelings of being unworthy, helpless, unattractive and having a lack of control over HS. These feelings can promote social isolation through avoidance of work and activities they used to enjoy, not talking about their disease due to embarrassment (Joachim & Acorn, 2000), and use of camouflage to avoid HS sites being

exposed. The pain and unpredictability of flares may also be a source of feelings of helplessness, irritation and sadness. These experiences can also impact sexual functioning, particularly if lesions are in anogenital regions as indicated by Matusiak et al. (2010).

As was found with anxiety, Pavon Blanco et al. (2018) demonstrated that illness beliefs had a stronger association with depression than disease severity. This is in accordance with previous research into psoriasis (Rapp et al., 1997; Scharloo et al., 2000) and other long-term conditions (Dempster, Howell & McCrory, 2015), and implies that how people with HS perceive their health has a stronger impact on psychological distress than how clinically severe their HS it.

4.3 Prevalence of Poor Quality of Life and Associated Factors in People with HS

Quality of life in HS was assessed in 91% of the eligible studies, with the DLQI being the most frequently used measure (90% of studies). In 63% of the studies that used the DLQI, HS had a very large impact on quality of life, and in the remaining 37% of studies HS had a moderate impact. Studies using other quality of life measures also indicated impaired quality of life, specifically in domains of pain, social functioning, self-care, general health, and emotional response. In studies comparing people with HS to healthy controls, 75% of these studies found that people with HS had a significantly poorer quality of life. In people with HS quality of life was also found to be poorer than people in the general population (Kluger et al., 2017).

Studies also compared HS to a range of other dermatological diseases and found participants with HS to have a poorer quality of life (in one study HS was the lowest of multiple diseases). Similar findings were also indicated in studies directly comparing HS to psoriasis. People with HS reported more distress and difficulties with social interaction, clothing choice, leisure activities and ability to study and work than people with psoriasis. These findings support research suggesting quality of life can be significantly poorer in people with HS both in comparison to the general population and other skin disorders (Gooderham & Papp, 2015; Kohorst, Kimball & Davis, 2015; Wolkenstein et al., 2007).

The relatively large standard deviations of DLQI scores across 16 of the studies, irrespective of methodological quality, indicate the wide-ranging impact of HS on quality

of life. This large variation in scores highlights the importance of examining factors that may explain the differences in how people cope with HS.

Demographic factors were not consistently related to quality of life. Similar to findings relating to depression in HS, age was not related to quality of life, and neither were education, employment and relationship status. Five studies (one rated as methodologically poor) found that females reported HS to have a very large or extremely large impact on their quality of life and males reported a lower impact, however three studies (two rated as methodologically poor) found no difference in gender. The quality ratings of these studies suggest that the findings of female gender as a factor may be more reliable and valid, and may be explained by the higher number of lesions in the lower abdomen in women than in men (Jemec, Heidenheim & Nielsen, 1996).

Psychosocial and lifestyle factors were found to be related to quality of life in 36% of the studies. As was found with anxiety and depression, Pavon Blanco et al. (2018) found that negative illness beliefs were related to poorer quality of life and shared some specific domains with those that related to anxiety and depression (beliefs about adverse consequences, large emotional response and lower treatment control). This supports previous research showing the impact of beliefs about negative consequences on health outcomes not only in other skin conditions (Cartwright, Endean & Porter, 2009) but also more generally in other long-term conditions (Dempster et al, 2015). This research shows that negative illness perceptions give rise to poorer coping which, in turn, leads to more adverse psychological and physical outcomes. For example, having more negative beliefs about how much their treatment can help their HS may reduce adherence to treatments and further impact quality of life. Higher anxiety and depression were also factors that directly related to poorer quality of life. This can be partly explained by vicious cycles maintained by negative illness beliefs, physical elements such as painful and malodourous lesions that may limit engagement in social activities, which can lead to feelings of helplessness and loneliness, and further avoidance of daily activities (Kouris et al., 2016).

Other psychosocial and lifestyle factors that were associated with poor quality of life were loneliness, poor sleep and sexual dysfunction (particularly in females), which is in keeping with psoriasis research (Ermertcan, 2009; Kouris et al., 2015; Ljosaa, Mork,

Stubhaug, Moum & Wahl, 2012). Females with HS may be more at risk of sexual dysfunction due the higher frequency of lesions in the lower abdomen than in men (Kurek et al., 2012). It is not surprising that loneliness was related to poor quality of life, as research has also found this in the general population with significant associations with depression, suicidal ideation and psychosis (Michalska da Rocha, Rhodes, Vasilopoulou & Hutton, 2017).

Although lifestyle factors such as smoking, BMI and obesity have been reported as risk factors influencing prognosis and severity of HS (Kromann, Ibier, Kristiansen & Jemec, 2014), these factors in addition to alcohol consumption were not related to poor quality of life. This finding is important as clinicians may target weight loss and smoking cessation, which can result in people with HS feeling blamed or stigmatised. It may be more beneficial for clinicians to target illness perceptions, loneliness, mood, anxiety, sexual dysfunction and sleep.

Clinical characteristics that were associated with poorer quality of life included disease severity, number of lesions, nape involvement, pain, itchiness, number of flares in last month, number of sick days in last three months, active disease and odour severity. Several of these findings are in line with previous studies (Jemec et al., 1996; Wolkenstein et al. 2007) and may be explained by the physical impact of HS on ability to engage in daily activities such as getting dressed, playing sports and generally moving around. This is particularly relevant to pain, which may be exacerbated by moving around and sweating (Kouris et al., 2016). Pain is a priority for research from the perspective of people with HS and their carers (Ingram et al., 2014), and evidence suggests that psychological intervention in skin diseases are less effective when accompanied by pain (Lavda, Webb & Thompson, 2012). Therefore, an increased focus on pain management in HS is warranted.

It is important to note that although greater disease severity was associated with poorer quality of life in HS, and considered the most important factor by Matusiak et al. (2010), negative illness beliefs accounted for more variance than disease severity in Pavon Blanco et al.'s (2018) study. This study by Pavon Blanco et al. (2018) was rated as having good methodological quality as opposed to Matusiak et al.'s (2010) study which was rated as poor, suggesting less risk of bias and further supporting the implications for

consideration of how people perceive their HS alongside clinical characteristics. Furthermore, the number of HS episodes, time until diagnosis, duration of first symptom, region at onset, and duration of HS were not significantly related to quality of life.

Approximately half of the total studies looked at how duration and age of onset of HS related to health outcomes. Only two of four studies measuring the relationship between age of HS onset and quality of life found significant correlations, and both indicated that younger age of onset was associated with poorer quality of life. Conversely, one study found that older age of onset was related to higher depression scores. These three studies linking age of onset with outcomes were all rated as methodologically poor and therefore should be interpreted with caution. All studies measuring the correlation between HS duration and quality of life and HS duration and depression found non-significant correlations. Furthermore, the number of HS episodes, duration of first symptom and region at onset were not significantly related to quality of life. The inconsistency of these findings of the how time that participants were exposed to HS related to health outcomes further indicates that clinical characteristics of HS may have less impact than may often be assumed. HS duration may also not always be accurately reported as there is frequently a delay to diagnosis, often around seven years (Revuz, 2009).

The study by Alavi et al. (2018a) demonstrated that different measures of quality of life can reflect contrasting findings, as has been shown in the measurement of depression elsewhere in the dermatology literature (Dowlatshahi et al., 2014). Studies using the DLQI indicated a significant difference in quality of life between males and females, whereas those using the Skindex-29 did not find a significant difference in quality of life between genders. Odour severity was a significant factor on the DLQI but non-significant on the Skindex-29. They also found the overall mean score for the impact of HS on quality of life on the DLQI was in the second highest impact category (very large impact), whereas the Skindex-29 was in the highest severity range (severe impact). These variations may be due to the different domains assessed in the DLQI compared to the Skindex-29, however this implies that scores on these measures should be interpreted with caution. There is a lack of clarity as to where the true values of overall quality of life and associated factors lie in this study.

Overall, the studies reviewed indicate that demographic, psychosocial, lifestyle and clinical factors are associated with poorer quality of life in HS. Sexual functioning and negative illness beliefs have been shown to account for more variance than disease severity in predicting quality of life. Similarly, a study of people with atopic dermatitis also found that psychological variables explained more variance in quality of life outcomes compared with demographic and clinical variables (Wittkowski, Richards, Griffiths & Main, 2004). Taken together, these findings reinforce that psychosocial factors should be considered in addition to clinical characteristics of HS when assessing quality of life.

4.4 Limitations of Previous Research

All studies that met inclusion criteria for this review were cross-sectional in design. This does not allow for conclusions to be drawn around causality or factors that may predict anxiety, depression and poorer quality of life over time. Furthermore, all participants were recruited from hospitals or HS clinics (apart from one study recruiting from blood donors) and were predominantly female, which may affect generalisability of findings. The fact that 87% of the studies had a majority of females is in line with statistics stated by Dufour et al. (2014) that the HS global prevalence is 3:1 ratio of females to males, however this also means that overall findings may not be applicable to males with HS. Risk of recruitment bias is also evident due to some samples being from tertiary/specialist clinics, where it is likely that HS is more severe.

Disease severity was measured using Hurley staging in 70% of the studies, indicating its popularity as a measure. These findings, however, may not be applicable to future research as new more dynamic measures of HS are being used in clinical practice (Kimball et al., 2014), especially when considering that the current review found that characteristics such as ‘active disease’ and number of lesions were associated with poorer quality of life. Indeed, recent research has criticized the use of Hurley staging due to inaccuracy about inflammatory activity in HS (Kimball et al., 2016), therefore the findings of the existing studies may or may not accurately reflect the true role of disease severity in its association with psychosocial variables.

This review only looked at studies that included the use of validated screening measures as opposed to studies only using criteria-based diagnoses of anxiety and

depression. Previous research has indicated differences in findings between screening instruments, as well as differences in findings between screening tools and use of diagnostic criteria (Machado et al., 2019). Therefore, the findings of this study may be overestimates of prevalence.

Throughout the quality assessment and data extraction process a number of methodological issues were evident. Four authors were contacted in order to gather information that was unavailable in their published studies. Agut-Busquet et al. (2018) were contacted to clarify the mean age and age range of their participants, Balieva et al. (2018) were contacted to clarify the total number of HS participants, their mean age and gender ratio, and Alavi et al. (2018b) were contacted to establish the mean DLQI score for people with HS. All authors replied and provided this information and gave consent for its use in this review. Kouris et al. (2016) were also contacted as it was not possible to access their materials and methods section for their article, however a response was not received therefore it was not possible to assess risk of bias and analysis for their study. It was also not possible to establish whether confounding variables had been adjusted or controlled for in nine studies, thus limiting replicability and confidence in drawing conclusions from the findings. There were three studies that used the same study cohort twice (Balieva et al., 2017; Kluger et al., 2017; Kurek et al., 2012), which did not impact their quality rating but should be considered when drawing conclusions from these studies.

4.5 Strengths and Limitations of the Current Review

This systematic review is the first to summarise research on anxiety, depression and quality of life in HS, as well as the first to consider factors associated with these outcomes. Limiting inclusion of studies to those that only use validated measures with overall/total scores of anxiety, depression and quality of life ensured more reliability and validity of findings that could be discussed more broadly than non-standardised measures with multiple index totals. The evidence base for psychological factors and outcomes in HS is minimal therefore findings can be used to inform both future areas for research but also clinical practice in terms of assessment and treatment.

There are several limitations of this review. Firstly, over half of studies used in this review were rated as fair in terms methodological quality and around a third of studies were rated as poor, therefore this review does not provide a robust summary of data. It is also possible that relevant information was not included in this review due to the exclusion of studies that were not focused on psychological outcomes, interventional studies, abstracts, reviews, communications and correspondence. Therefore, findings may not be representative of people with HS who are part of HS drug trials or more recent research that has not yet been published in peer reviewed journals. There were also three studies that were relevant but not possible to access. Stricter inclusion criteria that overall/total scores of outcomes were required meant that two relevant studies were excluded due to validated measures that were unable to be calculated as one score. A second independent reviewer completed the initial key search to check numbers of papers retrieved, assessed 20% of the full texts screened and 22% of the final eligible studies in terms of meeting inclusion/exclusion criteria. The second reviewer also assessed methodological quality of all studies and following discussion there was 100% inter-rater agreement between both reviewers. There is potential for subjective bias at these stages, particularly as the screening and eligibility stages were not completed by a second reviewer due to time constraints.

4.6 Implications for Future Research

Future research into HS would benefit from using longitudinal and cohort study designs in order to explore predictive factors of these outcomes. This will enable HS clinics to screen for risk factors for anxiety, depression and poorer quality of life in order to intervene at earlier stages. An increase in studies in to anxiety and depression in HS is also required due the currently limited evidence base. Due to the majority of studies having higher proportions of female participants, it may be useful for future research to also explore these outcomes in males specifically in order to establish findings that are more generalizable to male populations.

In terms of factors associated with anxiety, depression and quality of life in HS, it may be useful for future studies to use more recent disease severity measures, for example the HS-PGA or HiSCR in order to be applicable to current clinical practice and disease activity. Findings from Pavon Blanco et al.'s (2018) study indicate that illness

beliefs are significant factor in anxiety, depression and quality of life over and above disease severity therefore more research into this area will be useful as this can inform psychological treatments in HS. Moreover, it is recommended that these studies include measures of coping in order to understand the ways in which illness beliefs influence psychological outcomes. It was also noticed that in Janse et al.'s (2017) study that when measuring sexual distress, the authors controlled for question nine of the DLQI which related to sexual difficulties. This was not reported in the other studies assessing sexual functioning, therefore future research that considers sexual distress and functioning as a factor relating to quality of life may benefit from controlling for responses to question nine of the DLQI. Studies had also not controlled for pain when measuring outcomes which could significantly impact these outcome measures, therefore upcoming research may wish to consider including pain as a covariate. Furthermore, due to the lack of studies with good methodological quality, future research should ensure that key potential confounding variables, validated measures, HS severity and clear information on participant recruitment are included.

4.7 Implications for Clinical Practice

The results of this review indicate that anxiety, depression and quality of life should be routinely and regularly assessed in HS clinics, particularly as these health outcomes have also been shown to be associated with each other. Furthermore, the use of these self-reported outcomes will support clinical care pathways for people with HS to gain access to psychological care in addition to medical services. Findings regarding the factors that were associated with poorer outcomes indicate that psychosocial and lifestyle factors can have a significant impact on rates of anxiety, depression and poor quality of life. For example, assessment of illness beliefs (including greater adverse consequences, lower treatment control and larger emotional response) and sexual function may be beneficial to identify people who may be at risk of anxiety, depression and poorer quality of life, and to refer people with HS to psychological services if necessary. In addition to assessment, targeting illness perceptions and sexual function in interventions may support improved outcomes such as mood, anxiety and overall quality of life. In line with previous research (Sampogna et al., 2017), this review has demonstrated that with females in particular sexual dysfunction has been associated with poorer health outcomes, therefore awareness of this in healthcare professionals may allow for earlier identification of these factors.

Historically a larger emphasis may have been placed on clinical measurement of HS (e.g. disease severity and duration), however various studies have indicated that psychological factors such as illness beliefs, anxiety and depression may predict quality of life over and above disease severity. Duration of HS and age were not related to depression and quality of life in some studies further indicating that poorer health outcomes may not be linked with long-standing HS. Therefore, assumptions should not be made based on disease severity alone. Routine assessment of psychological and lifestyle factors will be important in addition to medical assessment, and in turn the development of interventions to improve psychological wellbeing.

4.8 Conclusions

To conclude, the results of this systematic review are consistent with past research stating that people with HS have higher prevalence rates of anxiety, depression and poorer quality of life. Although there was some variation in the findings, the prevalence rates in HS were found to be typically higher than controls, the general population and other skin diseases that were studied. For anxiety, the prevalence was found to be 27%, depression was mostly found to range between 35% and 38%, and quality of life was typically within the moderate to very large impact ranges. There were many different demographic, psychosocial, lifestyle and clinical factors related to these outcomes. Overall, this suggests that people with HS may benefit from being routinely assessed for anxiety, depression and poor quality of life, and also factors that may be indicate higher risk of these, including psychosocial and lifestyle factors (such as illness beliefs and sexual function), clinical factors (such as disease severity and pain), and awareness of demographic factors such as gender. Development of psychological interventions to target such factors with multidisciplinary care and support people at risk of or with poor health outcomes will be an important focus of future research.

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Appendix A – Search Terms

EMBASE: conducted on 28/01/19, n = 606
Second reviewer APB: conducted on 16/09/19, n = 787

1 exp suppurative hidradenitis/

2 Hidradenitis Suppurativa.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

3 Hidradenitis.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

4 Acne Inversa.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

5 exp anxiety/ or exp anxiety disorder/ or exp generalized anxiety disorder/

6 Anx*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

7 (Anxiety adj disorder$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

8 exp depression/

9 Mood.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

10 Depress*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

11 (Mood adj disorder$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

12 (Depress* adj disorder$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

13 distress.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

14 exp "quality of life"/

15 (Quality adj2 life).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

16 (Life adj quality).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

17 HRQL.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

18 QoL.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

19 (Well adj being).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

20 Well-being.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

21 Wellbeing.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

22 functioning.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

23 1 or 2 or 3 or 4

24 5 or 6 or 7

25 8 or 9 or 10 or 11 or 12 or 13

26 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22

27 24 or 25 or 26

28 23 and 27

29 limit 28 to (english language and yr="1990 -Current")

MEDLINE: conducted on 28/01/19, n = 245
Second reviewer APB: conducted on 16/09/19, n = 298

1 exp Hidradenitis Suppurativa/

2 Hidradenitis Suppurativa.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3 Hidradenitis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4 Acne Inversa.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

5 exp ANXIETY/ or exp ANXIETY DISORDERS/

6 Anx*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

7 (Anxiety adj disorder$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

8 exp DEPRESSION/

9 Mood.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

10 Depress*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

11 (Mood adj disorder$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12 (Depress* adj disorder$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

13 distress.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

14 exp "Quality of Life"/

15 (Quality adj2 life).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

16 (Life adj quality).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

17 HRQL.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

18 QoL.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism

supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

19 (Well adj being).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

20 Well-being.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

21 Wellbeing.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

22 functioning.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

23 1 or 2 or 3 or 4

24 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22

25 23 and 24

26 limit 25 to (english language and yr="1990 -Current")

PsychInfo: conducted on 28/01/19, n = 6
Second reviewer APB: conducted on 12/09/19, n = 6

1. Hidradenitis Suppurativa.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
2. Hidradenitis.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
3. Acne Inversa.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
4. exp ANXIETY DISORDERS/ or exp ANXIETY/ or exp GENERALIZED ANXIETY DISORDER/
5. anx*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
6. (Anxiety adj disorder$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
7. exp MAJOR DEPRESSION/ or exp "DEPRESSION (EMOTION)"/
8. Mood.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
9. Depress*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

10. (Mood adj disorder$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
11. (Depress* adj disorder$).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
12. distress.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
13. exp "Quality of Life"/
14. (Quality adj2 life).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
15. (Life adj quality).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
16. HRQL.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
17. QoL.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
18. (Well adj being).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
19. Well-being.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
20. Wellbeing.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
21. functioning.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
22. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 1 or 2 or 3
24. 22 and 23
25. limit 24 to (english language and yr="1990 -Current")

PubMed: conducted on 28/01/19, n = 671
Second reviewer APB: conducted on 16/09/19, n = 792

Mesh terms

“Hidradenitis Suppurativa”
“Anxiety”
“Anxiety Disorders”
"Depressive Disorder"
“Depression"
"Depressive Disorder, Major"
"Quality of Life"

Search

Search ((((("Hidradenitis Suppurativa") OR Hidradenit*) OR "Acne Inversa")) AND ((((((Anxiety) OR "Anxiety Disorders") OR Anx*)) OR ((((((“Depressive Disorder") OR "Depression") OR "Depressive Disorder, Major") OR mood) OR depress*) OR

distress)) OR (((((("Quality of Life") OR HRQL) OR QOL) OR Wellbeing) OR Well-being) OR "Well being") OR functioning))
Filters: Publication date from 1990/01/01 to 2019/12/31; English

CINAHL: conducted on 16/02/19, n = 66
Second reviewer APB: conducted on 16/09/19, n = 84

#	Query	Limiters/Expanders
		Limiters - Published Date: 19900101-20191231; English Language Search modes - Boolean/Phrase
S13	S9 AND S10	
		Limiters - English Language Search modes - Boolean/Phrase
S12	S9 AND S10	
S11	S9 AND S10	Search modes - Boolean/Phrase
S10	S3 OR S4 OR S5 OR S6 OR S7 OR S8	Search modes - Boolean/Phrase
S9	S1 OR S2	Search modes - Boolean/Phrase
S8	HRQL OR QOL OR Wellbeing OR well-being OR "well being" OR functioning OR "quality of life"	Search modes - Boolean/Phrase
S7	(MH "Quality of Life")	Search modes - Boolean/Phrase
S6	Depress* OR mood OR distress OR "depress* disorder*" OR "mood disorder*"	Search modes - Boolean/Phrase
S5	(MH "Depression")	Search modes - Boolean/Phrase
S4	Anx* OR "anxiety disorder*"	Search modes - Boolean/Phrase
S3	(MH "Generalized Anxiety Disorder") OR (MH "Anxiety")	Search modes - Boolean/Phrase
S2	“Hidradenitis Suppurativa” OR Hidradenit* OR “Acne Inversa”	Search modes - Boolean/Phrase
S1	(MH "Hidradenitis Suppurativa")	Search modes - Boolean/Phrase

Web of Science (Core Collection): conducted on 16/02/19, n = 328
Second reviewer APB: conducted on 16/09/19, n = 388

#5	#2 AND #1 Refined by: **[excluding]: PUBLICATION YEARS:** (1975) AND **LANGUAGES:** (ENGLISH) *DocType=All document types; Language=All languages;*
#4	#2 AND #1 Refined by: **[excluding]: PUBLICATION YEARS:** (1975) *DocType=All document types; Language=All languages;*
#3	#2 AND #1 *DocType=All document types; Language=All languages;*
#2	TS=(Anx* OR "Anxiety disorder*" OR Mood OR Depress* OR "Mood disorder*" OR "Depress* disorder*" OR distress OR "Quality of life" OR HRQL OR QoL OR "Well being" OR Well-being OR Wellbeing OR functioning) *DocType=All document types; Language=All languages;*
#1	TS=("Hidradenitis Suppurativa" OR Hidradenit* OR "Acne Inversa") *DocType=All document types; Language=All languages;*

EThOS: conducted on 16/02/19, n = 0
Second reviewer APB: conducted on 18/09/19, n = 0

"hidradenit* OR "acne inversa" AND "anx* OR depress* OR mood OR distress" AND "hrql OR qol OR "quality of life" OR wellbeing OR "well being" OR well\-being OR functioning"

OpenGrey: conducted on 16/02/19, n = 3 (none in English language)
Second reviewer APB: conducted on 18/09/19, n = 3 (none in English language)

Search: hidradenitis
Search: "acne inversa"

WorldCat: conducted on 16/02/19, n = 3
Second reviewer APB: conducted on 18/09/19, n = 3

(ti: hidradenit* OR (ti: hidradenitis and ti: suppurativa) OR (ti: acne and ti: inversa)) and (kw: anx* OR kw: depress* OR kw: mood OR kw: distress OR kw: qol OR kw: hrql OR (kw: quality and kw: life) OR kw: wellbeing OR kw: well-being OR (kw: well and kw: being) OR kw: functioning) and yr: 1990-2019 and la= "eng" and mt: deg.

Appendix B – Reasons for Exclusion at Screening and Eligibility Stages

Stage 1 (title and abstract review): 982

Excluded: 937

- Focused on other health conditions: 59
- Not focussed on psychological outcomes: 690
- Focussed on psychological outcomes, article type = Review / abstract / correspondence: 128
- Focussed on psychological outcomes, article type = Tool/guide development: 39
- Focussed on psychological outcomes, article type = Intervention: 12
- Focussed on psychological outcomes, sample = Mean age under 18: 5
- Focussed on psychological outcomes, article type = Case study: 2
- Focussed on psychological outcomes, article type = Qualitative: 2

Stage 2 (full paper review): 45

Excluded: 22

- Unable to access: 3
- Non-validated measures: 8
- Intervention: 5
- Not reporting HS separately from other conditions: 1
- Studies without an overall/total (validated) measure of QoL / anxiety / depression: 2
- Other: intervention and unable to access; unable to access and qualitative; thesis prior to publication: 3

Appendix C – Quality Assessment Method

The National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Institutes of Health, 2014)

Reference: Date of ax:

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

*CD, cannot determine; NA, not applicable; NR, not reported

Quality Rating (Good, Fair, or Poor)
Rater #1 initials:
Rater #2 initials:
Additional Comments (If POOR, please state why):

Appendix D – Quality Assessment Ratings

Table D1.

Quality Assessment Ratings

Paper reference	Qu.1	Qu.2	Qu.3	Qu.4	Qu.5	Qu.6	Qu.7	Qu.8	Qu.9	Qu.10	Qu.11	Qu.12	Qu.13	Qu.14	Quality rating
Agut-Busquet et al. (2018)	Y	Y	NA	Y	N	N	N	Y	Y	N	Y	NR	NA	NR	**Fair**
Alavi et al. (2015)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	**Fair**
Alavi et al. (2018a)	Y	Y	NR	Y	N	N	N	Y	N	N	Y	NR	NA	Y	**Fair**
Alavi et al. (2018b)	Y	Y	NR	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y	**Fair**
Balieva et al. (2017)	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NR	NA	Y	**Fair**
Balieva et al. (2018)	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NR	NA	Y	**Fair**
Calao et al. (2018)	Y	Y	N	Y	Y	N	N	Y	Y	N	Y	Y	NA	N	**Fair**
Janse et al. (2017)	Y	Y	N	Y	N	N	N	Y	Y	N	Y	NR	NA	NR	**Poor**
Kaaz et al. (2018)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	N	**Fair**
Katoulis et al. (2017)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	**Fair**
Kluger et al. (2017)	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	**Good**

Kluger et al. (2018)	N	Y	Y	Y	Y	N	N	Y	Y	N	Y	NR	NA	N	**Fair**
Kouris et al. (2016)	Y	N	NR	NR	N	N	N	Y	N	N	Y	NR	NA	Y	**Poor**
Kurek et al. (2012)	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	**Fair**
Kurek et al. (2013)	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y	**Good**
Matusiak et al. (2010)	N	N	NR	NR	N	N	N	Y	Y	N	Y	NR	NA	Y	**Poor**
Onderdijk et al. (2013)	Y	Y	Y	CD	N	N	N	Y	Y	N	Y	NR	NA	NR	**Fair**
Pavon Blanco et al. (2018)	Y	Y	NA	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y	**Good**
Rondags et al. (2019)	Y	Y	NA	Y	N	N	N	N	N	N	Y	NR	NA	N	**Poor**
Sartorius et al. (2009)	Y	Y	NR	Y	N	N	N	Y	Y	N	N	NR	NA	NR	**Poor**
Storer et al. (2018)	Y	Y	CD	N	N	N	N	Y	Y	N	N	NR	NA	Y	**Poor**
Theut Riis et al. (2019)	Y	N	CD	Y	N	N	N	N	Y	N	Y	NR	NA	Y	**Fair**
von der Werth & Jemec (2001)	Y	Y	Y	N	N	N	N	Y	N	N	Y	NR	NA	NR	**Poor**

PART II

Empirical Research Project

The Role of Disease Severity and Illness Perceptions in Predicting Quality of Life and Symptoms of Anxiety and Depression in People with Hidradenitis Suppurativa: A Longitudinal Study

---

Supervised by Professor John Weinman and Dr Mark Turner

Institute of Psychiatry, Psychology, and Neuroscience
King's College London

Candidate Contribution

I have contributed to this empirical project at each stage of the research including formulation of research questions, operationalising design, analysis and write-up. Based on my interest in Health Psychology and a baseline study that Professor John Weinman and Dr Mark Turner had supervised (Pavon Blanco et al., 2018), together we formulated three longitudinal research aims that followed-up on this study. I attended monthly to two-monthly supervision meetings with my supervisors from May 2018 to May 2020 and liaised with them via email and telephone in between these meetings. I contributed to the development and execution of the study design by liaising with my supervisors and Alicia Pavon Blanco to understand how the baseline project was operationalised and how she could establish which participants from her study had completed the required follow-up data. I attended a HS clinic team meeting with Dr Turner to inform the team of this proposal and consider how HS severity data could be collected in clinic for the second time point. I met with doctors in the HS clinic to formulate how they could extract HS severity data using the electronic patient record system. I applied for ethical approval from the NHS Health Research Authority and Health and Care Research Wales, and requested permission to implement the study from the Trust Research and Development Team. I contributed to data extraction by liaising with colleagues at Integrating Mental and Physical Healthcare: Research Training and Services (IMPARTS) to establish how they could gather my requested follow-up data, merge this with the data extracted by the doctors and send this to me securely. Once I had received this data I checked this against the inclusion/exclusion criteria and cleaned this for analysis. I contributed to statistical analysis by meeting with the King's College London Biostatistics and Health Informatics Service and attending two phone meetings with a statistician in the Health Psychology Department to design the analysis, and discuss execution and interpretation of this. I conducted, interpreted and wrote-up this analysis. I have also liaised with the HS Trust to explore how this research can be disseminated, and how service users can be involved in this process.

Table of Contents

List of Tables

List of Figures

Abstract

Background: Hidradenitis Suppurativa (HS) is a chronic skin disease presenting in the apocrine glands as inflamed nodules that often develop into fistulas, sinus tracts and scars. Research has found substantial rates of anxiety, depression and impaired quality of life in people with HS. These health outcomes have been linked to psychosocial factors including how people with HS perceive their illness (illness perceptions), and clinical factors such as disease severity. One study found illness perceptions were more strongly related to outcomes in HS than disease severity, however the study did not establish whether or not illness perceptions are predictive of outcomes over time.

Objectives: The first aim was to examine whether illness perceptions at baseline predict quality of life and symptoms of anxiety and depression over time, independently of disease severity. The second aim was to investigate the stability of illness perceptions over time, and if this is associated with health outcomes. The third aim was to explore the causal links between illness perceptions and depression over time.

Method: This was a longitudinal study of 135 participants with HS. The Brief Illness Perceptions Questionnaire (BIPQ), Generalised Anxiety Disorder-2 (GAD-2), Patient's Health Questionnaire-2 (PHQ-2), Dermatology Life Quality Index (DLQI) and Pain Visual Analogue Scale were completed at two time points (first appointment and a follow-up appointment). Doctors measured disease severity using Hurley staging.

Results: Multiple regressions indicated that illness perceptions explained a significant amount of variance in health outcomes over time, independently of disease severity when baseline health outcomes were not included in the models. HS severity explained very little of the variance in health outcomes across all models. Illness perceptions were stable over time, apart from beliefs about identity and concern about HS. Reductions in negative illness beliefs about consequences, timeline, personal control and concern were associated with improved health outcomes. Apart from personal control beliefs, depressive symptoms and illness perceptions mutually influenced each other over time.

Conclusions: Illness perceptions are better predictors of quality of life and symptoms of anxiety and depression over time than disease severity, most perceptions remain stable over time, and there is a mutual influence between depressive symptoms and illness perceptions over time. This has implications including routine assessment of illness perceptions in HS, and indicates the need for further research into interventions to modify illness perceptions with the aim of improving outcomes in HS.

1. Introduction

Hidradenitis Suppurativa (HS), also referred to as acne inversa, is a skin condition that is chronic and presents in the apocrine glands as inflamed nodules that usually progress into abscesses, sinus tracts (tunnels) and scarring (Kouris et al., 2016; Smith, Chao & Teitelbaum, 2010). The ratio of females to males with HS is approximately 3:1, typically presenting in early twenties and remaining active throughout thirties and forties (Dufour, Emtestam & Jemec, 2014). Reports of global prevalence of HS range from 0.03% to 8%, however this may be underreported due to various reasons such as misdiagnosis, the average time from initial symptoms to diagnosis being 7 years, or shame (Jemec, 2012; Jemec & Kimball, 2015; Saunte et al., 2015; Slade, Powell & Mortimer, 2003). In order to meet diagnostic criteria for HS typical lesions must be present (such as painful nodules, abscesses, draining sinus and scars), be chronic and recurrent, and mainly present in more than one of the following areas: groin, axillae, perineal region, buttocks and infra- and intermammary folds (van der Zee & Jemec, 2015; Vinding et al., 2014).

1.1 Disease Severity

HS exists at different levels of severity and there are different measures used to assess this including Hurley staging (Hurley, 1989), HS-Physician's Global Assessment (HS-PGA; Zouboulis et al.., 2015; Kimball et al., 2012), Modified Sartorius Score (Sartorius, Emtestam, Jemec & Lapins, 2009; Sartorius, Lapins, Emtestam & Jemec, 2003), and the International Hidradenitis Suppurativa Severity Scoring System (Zouboulis et al., 2017), and the Hidradenitis Suppurativa Clinical Response (HiSCR; Kimball et al., 2016). Hurley staging has been widely used in research and clinical practice; this classification of severity is stated as follows (Hurley, 1989):

- Stage I: Abscess formation, single or multiple, without sinus tracts and cicatrization (the process of wound healing that produces scar tissue)
- Stage II: Recurrent abscesses with tract formation and cicatrization, single or multiple, and widely separated lesions
- Stage III: Diffuse or near-diffuse involvement or multiple interconnected tracts and abscesses across the entire area (Hurley, 1989)

The prevalence of each stage is uncertain. Studies have reported that Hurley stages 1 (24-68%) and 2 (28-54%) are most common whereas stage 3 (2-29%) is less common (Canoui-Poitrine et al., 2019; Delany et al., 2017; Katoulis et al., 2017; Matusiak, Bieniek & Szepietowski, 2009; Schrader, Deckers & van der Zee, 2014; Vazquez, Alikhan, Weaver, Wetter & Davis, 2013). In 30% of cases mild forms of HS may become more severe over time (Kromann et al., 2014).

Treatment varies according to the severity of HS; currently there is no cure and there is a lack of high-quality evidence for HS therapy (Elkin, Daveluy & Avanaki, 2020; Ingram, 2016; Zouboulis et al., 2015). In the UK, topical antiseptics and antibiotics, and oral immunomodulators and retinoids are prescribed for HS in an escalating sequence (Ingram, 2016). Several randomised controlled trials have assessed efficacy of anti-tumour necrosis factor-alpha (TNFα) therapies, which inhibit the protein TNF-alpha and are prescribed for severe HS (Ingram, 2016). For isolated nodules incisions and draining may be performed, whereas for extensive HS broader excision may be performed and has lower risk of recurrence (Ingram, 2016). Body mass index and smoking are associated with disease severity (Sartorius et al., 2009) therefore lifestyle changes are recommended in terms of obesity and smoking, with strong associations between HS and likelihood of spontaneous remission in non-smokers (Ingram, 2016; van der Zee, van der Woude, Florencia & Prens, 2010). Disease severity has also been found to reduce following bariatric surgery (Thomas, Gordon & Mortimer, 2014).

1.2 Psychosocial Impact of HS

There has been research into the psychosocial impact that HS can have. The abscesses can be painful and malodorous, presenting in areas such as the groin, armpits and anogenital regions. This has been found to elicit feelings of embarrassment, shame, sadness and anger about appearance and smell, and impact on romantic relationships (Esmann & Jemec, 2011; Keary, Hevey & Tobin, 2019). Research has also indicated that there are higher rates of unemployment and sick leave than the general population (Alkikhan, Lynch & Eisen, 2009).

Anxiety

A recent systematic review of 10 studies by Machado et al. (2019) found the prevalence rate for anxiety in HS was 4.9%, whereas other studies have found prevalence rates of 6.9% and 27% (Huilaja et al., 2018; Pavon Blanco, Turner, Petrof & Weinman, 2018). Anxiety has also been found to be more prevalent in HS than other dermatological conditions and the general population (Huilaja et al., 2018; Shavit et al., 2015). Symptoms of depression and higher disease severity have been found to be associated with anxiety in HS (Kouris et al., 2016; Kurek et al., 2013). These findings indicate that further research is required into depression and anxiety in HS and factors including disease severity, that may be predictive of these health outcomes.

Depression

Prevalence of depression in HS has been found to vary across research. Machado et al.'s (2019) systematic review found the prevalence to be 16.9% (26.8% in studies using screening tools), whereas other studies have found prevalence rates over 35% (Kluger, Ranta & Serlachius, 2017; Kurek, Peters, Sabat, Sterry & Schneider-Burrus, 2013; Pavon Blanco et al., 2018). HS has also been found to have a higher prevalence of depression than healthy control groups and the general population (Kouris et al., 2016; Kurek et al., 2013; Shavit et al., 2015) and other dermatological conditions (Huilaja, Tiri, Jokelainen, Timonen & Tasanen, 2018; Onderdijk et al., 2013). Various factors have been found to be associated with depression in HS including pain, sick days, age of onset, gender, quality of life, anxiety and sexual distress. (Kluger, et al., 2017; Kurek et al., 2012; Matusiak et al., 2010; Onderdijk et al., 2013). There are conflicting studies regarding the association of disease severity and depression in HS. Several studies indicate higher severity being related to higher depression scores (Kouris et al., 2016; Kurek et al., 2013; Matusiak et al., 2010; Onderdijk et al., 2013), whereas others have not found significant correlations (Kluger et al., 2017). There has also been debate about proinflammatory cytokines involved in HS development, also impacting the development of depression (Goldstein, Kemp, Soczynska, & McIntyre, 2009; Kelly & Prens, 2016; Kohler et al., 2017; van der Zee et al., 2011).

Quality of Life

Quality of life has also been widely researched in HS. It has been measured using different tools and constructs, including aspects of psychological, physical and social

functioning (de Korte, Sprangers, Mombers, Bos & Sprangers, 2004). One of the more commonly used patient-reported outcome measures in dermatological conditions is the Dermatology Quality of Life Index (DLQI; Finlay & Khan, 1994). This comprises of questions regarding symptoms, feelings, sport, daily activities, leisure, work/study, relationships and treatment. Research has indicated that people with HS have higher rates of impaired quality of life than the general population (Kluger et al., 2017). Studies using measures such as the DLQI have found HS to have a very large impact on peoples' lives (Alavi et al., 2018; Balieva et al., 2018; Calao et al., 2018). They have also found higher rates of impairment than other skin disorders including atopic dermatitis and psoriasis (Matusiak et al., 2010).

Psychosocial and lifestyle factors such as anxiety, depression, loneliness, poor sleep and sexual dysfunction have been found to be associated with poorer quality of life in people with HS (Janse et al., 2017; Kaaz, Szepietowski & Matusiak, 2018; Kouris et al., 2016). Demographic factors such as gender (being female) and later age of onset were associated with poorer quality of life (Kluger et al., 2017; Matusiak et al., 2010), whereas other studies did not find these to be linked (Alavi et al., 2018; Kurek et al., 2012). Clinical characteristics such as disease severity, odour severity and itchiness have also been linked with impaired quality of life (Alavi et al., 2015; Alavi et al., 2018; Onderdijk et al., 2013). Despite research demonstrating significant associations between HS severity and quality of life, Onderdijk et al. (2013) found a borderline significant correlation with a high degree of variability. This research has demonstrated evidence of impact HS has on quality of life but has largely used cross-sectional designs. Longitudinal research that predicts the impact of HS and associated factors on quality of life is required.

Pain

Previous research has found that pain causes considerable distress in people with HS (Keary et al., 2019), and is positively correlated with the impact of HS on quality of life (Wolkenstein et al., 2007). A qualitative study by Keary et al. (2019) found that people with HS reported that others were unable to understand their pain and therefore dismissed it, which led them to feel angry and isolated. These findings indicate that both in research and clinical practice pain should be considered when assessing the impact of HS on health outcomes.

1.3 Illness Perceptions

Psychological research has used social cognitive models to understand the processing of information by patients regarding their illness. The Common-Sense Model (CSM) by Leventhal, Meyer and Nerenz (1980) proposes that individuals who experience new health threats build cognitive and emotional models of their illness (illness perceptions) derived from 'lay' information they have about the illness, information from authoritative or significant others, and their current experience with the illness (Leventhal, Nerenz & Steele, 1984). Schematic and conceptual illness representations are formed through concrete evidence (e.g. body symptoms) and abstract information (the symmetry rule), linking symptoms to diagnosis labels stored in semantic memory (Leventhal, 1990).

Research has identified five main components of these illness models, including beliefs about cause, timeline, control or cure, consequences and identity (Petrie & Weinman, 2006). Cause indicates the beliefs about factors that have caused the illness, and can strongly influence choice of treatments and emotional responses (Petrie & Weinman, 2006). Timeline represents beliefs about the course and time scale of the illness (e.g. acute or chronic), and can influence adherence to treatments. Controllability or cure refer to the beliefs about personal control over the illness (e.g. efficacy of coping behaviours) and how well it is controlled by treatment (Lau & Hartman, 1983). Higher control beliefs are often linked with shorter timeline beliefs (Petrie & Weinman, 2006). Consequences can refer to the impact of the illness on factors such as lifestyle, family and work, and can reflect the subjective views of the illness severity which may not be in line with clinical measures of severity (Petrie & Weinman, 2006). Identity refers to the label individuals have for their illness and the symptoms they associate with it, however beliefs about symptoms caused by the illness may differ from what is medically indicated (Petrie & Weinman, 2006). The Brief Illness Perception Questionnaire (Broadbent, Petrie, Main & Weinman, 2006) was created in order to provide clinicians with a theoretically-derived and rapid picture of how patients view their illness using these components. This measure also incorporates emotional components including emotional response and concern about the illness, in addition to understanding of the illness (Broadbent et al., 2006).

In order for individuals to reduce the threat of their illness and their emotional response to it, their coping strategies and health outcomes are guided by their cognitive

model of illness perceptions (Leventhal et al., 1980; Petrie & Weinman, 2006). Their appraisal of their coping strategies may then change their illness perceptions and subsequent coping responses in a continuous feedback loop (Broadbent et al., 2006; Leventhal et al., 1980). A meta-analysis of 45 empirical studies measuring illness perceptions from the CSM (Leventhal, 1980) in 23 illnesses and conditions provided support for the construct and discriminant validity of these components and for measures using these components (Hagger & Orbell, 2003). Hagger, Koch, Chatzisarantis and Orbell (2017) conducted a further meta-analysis of 254 studies on chronic illnesses and found that although coping responses partially account for the effect of illness representations on outcomes, cognitive and emotional representations impact outcomes independently of coping.

Illness Perceptions and Health Outcomes

There is increasing evidence showing that illness perceptions across various chronic illnesses including heart failure, psoriasis, rheumatoid arthritis, and chronic obstructive pulmonary disease are significantly related to anxiety, depression and quality of life outcomes (Morgan, Villiers-Tuthill, Barker & McGee, 2014; Scharloo et al., 1998, 2000). Gray and Rutter (2007) found that, in people with chronic fatigue syndrome, illness perceptions about greater treatment control and lower identity and emotional response were associated with better quality of life. Hagger and Orbell (2003) found that beliefs in a chronic timeline, serious consequences and a strong illness identity were associated with decreased psychological well-being and social functioning, and in Hagger et al.'s (2017) review consequences and identity were consistent positive predictors or greater distress and poorer well-being. Scharloo et al. (1998) and Kemp, Morley and Anderson (1999) also found identity and perceptions of symptoms explained the most overall variance in illness outcomes. High perceived control over the illness has been strongly related to better psychological well-being and reduced depression and anxiety (Bradley, Lewis, Jennings & Ward, 1990; Hagger et al., 2017; Hagger & Orbell, 2003; Morgan et al., 2014; Shillitoe & Christie, 1990). Chilcot et al. (2013), however, found that personal control was not associated with depression trajectory in people with end-stage renal disease. Emotional representations have also been positively associated with distress and anxiety, and negatively associated with well-being (Hagger et al., 2017; Morgan et al., 2014). Overall, these findings suggest that individuals are more likely to experience better well-being and less distress if they perceive their illness as under

control, treatable, and having a lower effect on their life, and if they are able to reduce their emotional response and attribution of symptoms to their illness (Hagger et al., 2017).

Illness Perceptions and Disease Severity

Anxiety, depression and quality of life have been found to have stronger associations with illness perceptions than disease severity in conditions such as heart failure and multiple sclerosis (Jopson & Moss-Morris, 2003; Morgan et al., 2014). Based on these findings, a recent research study by Pavon Blanco et al. (2018) found that illness perceptions about HS explained a greater amount of variance in anxiety, depression and quality of life outcomes in comparison to demographics and disease severity. Pavon Blanco et al. (2018) also found that there was a lack of association between disease severity and illness perceptions, indicating a weak link between them and between clinical measures and patients' evaluations of HS. Compared to cohorts with asthma, diabetes and myocardial infarction, the participants with HS in this study demonstrated more negative beliefs about the consequences, experience of symptoms, concern about HS and a stronger emotional response, and less negative beliefs about personal and treatment control (Broadbent et al., 2006; Petrie, Perry, Broadbent & Weinman, 2012; Pavon Blanco et al., 2018). Emotional response was significantly correlated with symptoms of anxiety and impaired quality of life (Pavon Blanco et al., 2018). The perception of negative consequences was the most significant contributor to the health outcomes, and treatment control explained a significant amount of variance in depression and quality of life scores. Thus, illness perceptions about HS may be a more effective indicator of people at risk of poorer health outcomes as opposed to the traditional explanatory variable of disease severity.

Longitudinal Impact of Illness Perceptions and Disease Severity

Pavon Blanco et al.'s (2018) study was the first to explore the nature and impact of illness perceptions in HS, however the cross-sectional design did not allow for exploration of the predictive utility of illness perceptions over time. There is longitudinal research into other chronic illnesses including coronary artery disease and head and neck cancer, that has found illness perceptions to be predictive of depressive symptomatology over time (Llewellyn, McGurk & Weinman, 2007; Stafford, Berk & Jackson, 2009). Perceptions of illness have also been found to be strong predictors of recovery independently of illness severity in myocardial infarction and mild head injury (Petrie et

al., 1996; Whittaker, Kemp & House, 2007). Broadbent, Petrie, Ellis, Ying and Gamble (2004) found that in people with myocardial infarction (MI) recovery was more strongly predicted by their drawings of damage to their hearts than medical indicators (troponin-T levels). When participants were asked to draw hearts over 6 months after MI the size of the heart predicted cardiac anxiety (Broadbent, Ellis, Gamble & Petrie, 2006). Prospective dermatological studies have found similar evidence; Scharloo et al. (2000) demonstrated that illness beliefs explained more variation in disability, psychological distress and psoriasis-related stresses than disease severity over time.

Conversely, Wahl et al. (2014) showed that people with greater disease severity held stronger illness perceptions about the consequences, timeline and emotional impact of psoriasis, indicating that disease severity and these illness perceptions may not be independent of each other in this dermatological condition. Further longitudinal research is required in order to explore whether illness perceptions and disease severity are independent of each other in predicting outcomes in HS.

Stability of Illness Perceptions and Relation with Depression Over Time

Research into the stability of illness perceptions over time has not yet been explored in HS. The CSM (Leventhal et al., 1980, 1984) suggests that there are two processes which influence the development of illness perceptions. The first implies that when individuals are first aware of health threats they tend to perceive them as acute and therefore treatable with limited duration (Fischer et al., 2010). In chronic illnesses, perceptions of the timeline of the illness shift from acute to chronic. The second process is the reshaping of illness perceptions based on the outcomes of treatment (Leventhal, Brissette & Leventhal, 2003). Findings from previous research into chronic conditions have been varied. Cardiac studies have indicated that understanding of the illness (coherence) and perceptions of the timeline increase over time, whereas emotional responses and perceived controllability decrease (Fischer et al., 2010; Petrie & Weinman, 1997). Diabetes research found similar findings apart from controllability which remained stable over time (Lawson, Bundy & Harvey, 2008). Studies into irritable bowel syndrome and lower back pain have found all illness perceptions to remain stable over time (Foster et al., 2008; Rutter & Rutter, 2007). Studies are limited in this area and to date research has not been conducted to investigate whether illness perceptions change

over time in an HS population, and whether change in illness perceptions has an impact on health outcomes.

Leventhal et al.'s (1980) model is a parallel processing model with a cognitive and emotional pathway, however, most CSM research has focused on the impact of cognitions on emotional and behavioural outcomes (Revenson & Diefenbach, 2019). Leventhal and Scherer (1987) suggested that emotion and cognition are "always intertwined" in emotional behaviour and experience, and to find emotional responses completely independent of cognitive responses or perceptions would be rare. This emphasises the importance of investigating further the interaction between illness perceptions and emotions. Depression is highly prevalent in HS, and the strong associations that have been found between illness perceptions and depression have mainly been derived from cross-sectional studies. Longitudinal studies in other long-term conditions such as Chilcot et al. (2013) have focused on the direction of illness perceptions as predictors of depression, however, it is possible that depression may be determining illness perceptions as much as the reverse direction.

There is extensive literature regarding the direction of influence between negative cognitions and depression (Kindt, Kleinjan, Janssens & Scholte, 2015; Rush, Weissenburger & Eaves, 1986; Teasdale, 1983), however this has not been examined in relation to beliefs about illness. Beck's (1967) cognitive model suggests that the negative cognitive triad (negative thinking about the self, world and future) has a causal role in how depression develops and is maintained, and that maladaptive schemata may indicate a vulnerability to depression. Research indicates that mood can influence how accessible positive and negative cognitions are; depression may increase access to negative cognitions and decrease accessibility of positive cognitions (Bower, 1981; Teasdale, 1983; Tversky & Kahneman, 1974). As a result, this may increase negative memories and attention towards negative elements of current experiences, reduce positive expectations and interpretations of outcomes and experiences of coping, thus reinforcing feelings of sadness (Beck, Rush, Shaw & Emery, 1979; Clark, Beck & Alford, 1999). This may impact behavioural responses and subsequent appraisal of their coping strategies, feeding into Beck's (1967) negative cognitive triad, and thus increasing symptoms of depression (Teasdale, 1983). This demonstrates a vicious cycle between cognitions and depression, which may also be indicated between illness beliefs and depression. Leventhal et al.

(1980) and Petrie and Weinman (2006) have suggested that coping strategies and health outcomes are guided by perceptions of illness, and that this model is dynamic in that appraisal of coping informs the development of illness perceptions in a feedback loop. Therefore, it is possible that health outcomes such as depression can feedback and influence the formation of illness perceptions.

Selectively attending to negative stimuli and interpreting ambiguous information as having negative meaning are automatic processes found to maintain depression (Disner, Beevers, Haigh & Beck, 2011; Phillips, Hine & Thorsteinsson, 2010). Orbell and Phillips (2019) have provided evidence that implicit processes of attentional and interpretation bias are possible antecedents of illness representations. Therefore, it is possible that depression may also impact illness perceptions over time, and research is required to examine this as it is a current gap in the literature of HS and other chronic illnesses.

1.4 Study Aims and Hypothesis

To date, most research has focused on clinical characteristics of HS relating to health and lifestyle outcomes (Revuz et al., 2008; Sartorius et al., 2009). Research is limited in exploring illness perceptions in HS, and has not investigated the extent to which illness perceptions are predictive of health outcomes over time in HS. Therefore, the first aim of this study is to follow-up on Pavon Blanco et al.'s (2018) study to examine whether illness perceptions at baseline predict quality of life and symptoms of anxiety and depression over time, independently of HS severity. The hypothesis is as follows:

- **Hypothesis:** Illness beliefs assessed at first presentation to the clinic will be a stronger predictor of longitudinal outcomes (quality of life and symptoms of anxiety and depression) than HS disease severity.

The second aim of the project is to investigate the stability of illness perceptions over time, and if this is associated with these health outcomes. Findings from this research are intended to be generalisable to the wider HS community in the UK and will indicate if illness perceptions are independent of disease severity in explaining and predicting outcomes. This will provide implications for the identification of people with HS who may be at higher risk of poor health outcomes (depression, anxiety and quality of life).

The findings will also inform the development and use of psychological intervention in HS alongside dermatological treatment. There has been research into interventions targeting cognitive change through modification of illness perceptions in other health conditions (Broadbent, Ellis, Thomas, Gamble & Petrie, 2009; Petrie, Cameron, Ellis, Buick & Weinman, 2002; Petrie et al., 2012), and it is hoped that findings from this study will further the development of psychological interventions in order to optimise health outcomes for people with HS.

There is growing evidence that illness perceptions play a significant role in influencing psychological outcomes, however, the bi-directional link between illness perceptions and mood has not yet been explored. Prospective research is required to determine the direction of influence; therefore, the third aim of the project is to explore (i) the extent to which illness perceptions predict symptoms of depression over time and (ii) the extent to which symptoms of depression predict illness perceptions over time in people with HS. Findings will provide implications for identifying people who may be at risk of developing negative illness perceptions about HS which could impact on health outcomes. This may further inform interventions for these at-risk groups to target mechanisms that maintain both directions of influence. The project's aims therefore also inform multidisciplinary care for people with HS and development of care pathways into services targeting symptoms of depression.

2. Method

2.1 Design

This study is longitudinal in design, using data collected routinely in the HS tertiary clinics at a London teaching hospital. A portion of the data is collected for electronic patient records and the remaining data is gathered through Integrating Mental and Physical Healthcare: Research Training and Services (IMPARTS).

The project is following up on 164 participants from a cross-sectional baseline study that was conducted between 2014 and 2015 by Pavon Blanco et al. (2018). The

information collected at baseline was gathered again from their first follow-up appointment that they had completed all the measures at.

2.2 Ethical Approval and Informed Consent

Ethical approval was granted by the NHS Health Research Authority (HRA) and Health and Care Research Wales (HCRW), and permission to implement the study was granted from the Guy's and St Thomas' (GSTT) NHS Foundation Trust Research and Development (R&D) Team. King's College London Research Ethics Team were approached and confirmed that ethical approval was not required. This study was deemed as Research Ethics Committee (REC) exempt as the project is limited to the use of data collected routinely in the normal care of participants, and is anonymised to the researcher outside of the direct health care team. A non-substantial amendment was made to the protocol following a change in the research team members. This was approved by the HRA and GSTT R&D (see Appendices A - F for approval confirmations).

The screening measures used to assess illness perceptions, pain, symptoms of anxiety and depression, quality of life, age and gender are routinely collected in the HS clinic as part of the IMPARTS initiative. Approval to access to this IMPARTS data was granted by the IMPARTS Oversight Committee (see Appendix F for approval emails). In keeping with IMPARTS ethical approval, formal informed consent was not given by participants, however they were able to opt out (IMPARTS Database REC reference: 18/SC/0039). Informed consent was not sought from participants to gather HS severity data as this was collected by direct members of the health care team and pseudonymised by IMPARTS before the researcher outside of the direct health care team had access to this.

2.3 Inclusion and Exclusion Criteria

Participants were required to have a diagnosis of HS, with data available in the patient notes via the direct health care team. Participants were included if they had participated in Pavon Blanco et al.'s (2018) study (time point 1) and had a follow-up screening date with all the self-report questionnaires required for the study completed (time point 2). All baseline data was gathered at each participants' first appointment at the HS clinic.

Participants were excluded if they had not completed all measures at baseline and follow-up, were unable to read English, were under the age of 18, had 'opted out' of their IMPARTS data being used for research, and if HS severity could not be determined from their notes.

2.4 Measures

2.4.1 Clinician-Rated HS Severity

HS severity was measured using Hurley's staging system (Hurley, 1989). Hurley staging is a visual classification of severity using a three-stage scoring system: stage I (mild), II (moderate) and III (severe). It measures static features including fistulas and scars, and patients' stage of severity can increase (severity can become worse). Hurley staging was used as it is a well-established measure of HS severity that was used routinely in the HS clinic and allowed this study to follow-up on the baseline cohort of participants in Pavon Blanco et al.'s (2018) research.

2.4.2 Illness Perceptions

Illness perceptions were measured using the Brief Illness Perceptions Questionnaire (BIPQ: Broadbent et al., 2006). This is a valid and reliable self-report measure evaluating cognitive and emotional representations of illness. This 9-item scale assesses the following domains: perceived health outcomes of the illness (*consequences*); perceived duration of the illness (*timeline)*; perceived control over the illness (*personal control and treatment control*); illness label and related symptoms (*identity*); emotional response to the illness (*concern and emotional response*); illness comprehensibility (*understanding*); and perceived causes of the illness. The causes component is not routinely collected in the HS clinic due to its qualitative format, therefore it was not collected at baseline or follow-up for this study. Items are rated on a 10-point scale; higher scores indicate a more threatening perception of the illness. The Cronbach's alpha for the BIPQ in this sample was $\alpha = .673$ at baseline which indicates acceptable reliability, and $\alpha = .750$ at follow-up which is good reliability (Kline, 2013). It has nonetheless been recommended that each item value is considered in analysis; as opposed to the overall score (Broadbent et al., 2015). This questionnaire is administered on a six-monthly basis in the HS clinic.

2.4.3 Depression, Anxiety, Quality of Life and Pain

Symptoms of depression was screened using the validated Patient's Health Questionnaire-2 (PHQ-2: Kroenke, Spitzer & Williams, 2003), which is a self-report measure for assessing depressive symptoms within the past 2 weeks. The Generalised Anxiety Disorder-2 (GAD-2: Kroenke, Spitzer, Williams, Monahan & Löwe, 2007) was used to screen for anxiety symptoms. It is a validated self-report measure for assessing symptoms of GAD in the past two weeks. Previous research has indicated that the PHQ-2 and GAD-2 have been reliable measures in chronic illness populations including lung cancer and cardiovascular disease (Celano et al., 2013; Randall et al., 2013). Items are rated on a 4-point scale from 0 (not at all) to 3 (nearly every day), with scores up to 6 on each. Higher scores indicate higher symptom severity; the recommended cut-off point ($\geq$ 3) represents clinically significant depression or anxiety (Kroenke et al., 2010). It should be noted that these tools are used as screening measures not clinical diagnostic tools; the cut-off points are used to prompt completion of the full PHQ-9 / GAD-7 measures or a clinical interview to determine disorders and whether referral or treatment is warranted (Kroenke et al., 2007; Kroenke et al., 2010). The Cronbach's alpha for the GAD-2 was α = .893 at baseline and α = .877 at follow-up indicating good reliability (Kline, 2013). For the PHQ-2 the Cronbach's alpha was α = .780 at baseline and α = .856 at follow-up also indicating good reliability (Kline, 2013).

The 10-item Dermatology Life Quality Index (DLQI: Finlay & Khan, 1994) is a self-report questionnaire that was used to measure quality of life in dermatological illnesses. There is a maximum score of 30, with higher scores indicating poorer quality of life. Cut-off points for the DLQI stated by Hongbo, Thomas, Harrison, Salek and Finlay (2005) are as follows: 0 - 1 (no effect on patient's life), 2 - 5 (small effect), 6 - 10 (moderate effect), 11 - 20 (very large effect), and 21 - 30 (extremely large effect). The Cronbach's alpha in for the DLQI was α = .723 at baseline and α = .744 at follow-up, indicating good reliability (Kline, 2013).

Pain severity was measured using a visual analogue scale (Jensen & Karoly, 2011); patients provided a single score from 0 - 100 (no pain – most severe pain possible).

2.5 Procedure

In the HS clinics at a large teaching hospital in London, patients are administered the PHQ-2, GAD-2, DLQI and Pain VAS on a tablet device by registered nurses at every clinic visit, and the BIPQ is administered every 6 months. The Electronic Patient Record (EPR) is linked to the tablets through the IMPARTS initiative.

A previous researcher with an honorary appointment with the NHS Trust screened the original 211 participants in Pavon Blanco et al.'s (2018) sample and identified 164 participants with a follow-up appointment that they had completed all questionnaires at. These follow-up dates were added to an excel spreadsheet containing each participant's hospital number and baseline screening date. Two doctors in the direct health care team used patient letters in EPR to extract each participant's Hurley stage at both time points. They matched these to the hospital numbers and screening dates in the spreadsheet, and sent it securely to IMPARTS. IMPARTS then matched these participants with their screening measure data, and replaced all patient identifiers with a study ID code. This spreadsheet was then sent securely to the researcher outside of the direct health care team for analysis. A code-break spreadsheet providing the individual link back from the pseudoanonymised data sheet was sent to the two doctors in the direct health care team. This was kept in a separate password protected folder on an NHS server, accessible to the two doctors only.

2.6 Statistical Analysis

Data analysis was conducted using Statistics Package for the Social Sciences (SPSS) for Windows version 25. There were 27 participants excluded from this study due to missing data on pain severity and/or HS severity at follow-up and one participant being under age 18. G*Power 3.1 was used for post-hoc power analysis. A sample size of 135 achieved a statistical power of 80% and 99% to detect a medium (0.15) and large (0.35) F^2 effect size respectively at .05 alpha level. It should be noted that this sample size is smaller than recommended for multiple regression (requires > 150) to detect a medium effect with 15 predictors (Cohen, 1988).

To support statistical analysis the following disease severity groups were clustered: participants who were recorded on EPR as stage I or I/II are referred to as

'mild', participants recorded as stage II or II/III are referred to as 'moderate' and participants recorded as stage III will be referred to as severe throughout this study.

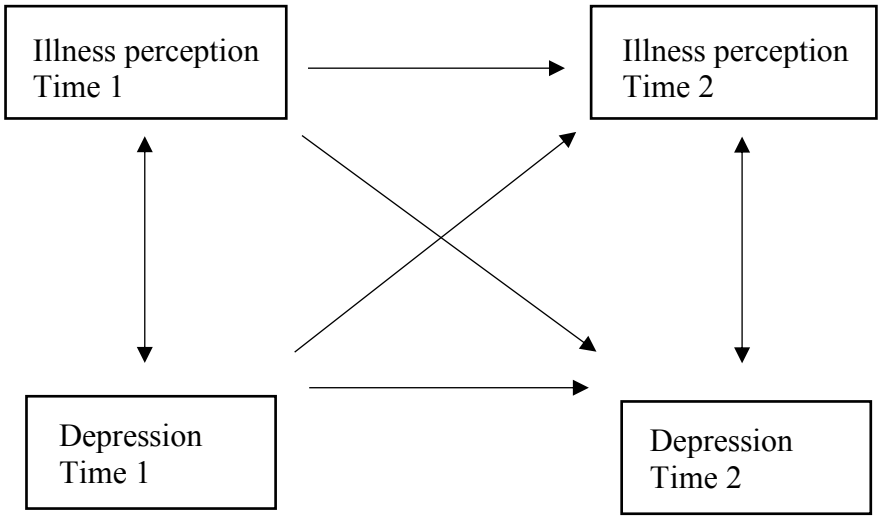
Relationships between illness perceptions at time 1 and health outcomes at time 2, independent of HS severity, were analysed by conducting hierarchical multiple regressions with bias-accelerated bootstrap (1000 samples) on each dependent variable (depression, anxiety and quality of life). In order to control for possible confounders step 1 of the regression analyses included gender, age (baseline) and pain (baseline). In order to investigate the predictive ability of illness perceptions when baseline anxiety, depression and quality of life are also accounted for, additional regressions were run for each outcome with the baseline measure of the outcome also included as a predictor at step 1. Two dummy variables were created for the three baseline Hurley stages and entered in at step 2. Illness perceptions at baseline were entered into step 3 of the analyses. Statistical significance was defined as $p < .05$.

Stability of illness perceptions over time were analysed by running a Friedman's two-way analysis of variance by ranks to identify any statistically significant changes between baseline and follow-up. Wilcoxon-signed rank tests were used to follow-up significant findings using a Bonferroni correction ($p < .0167$ significance level). The association between change scores for illness perceptions over time and outcomes were analysed using Spearman's rho correlation coefficients.

To explore the bidirectional relationship between illness perceptions and symptoms of depression over time, Spearman's rho were first conducted to identify illness perceptions that had correlations with symptoms of depression of .3 and over. A two-wave cross-lagged panel design (Kessler & Greenberg, 1981) was then used to measure the extent to which the cross-lagged relationships between the selected illness perceptions and symptoms of depression predict each other across times one and two (Figure 1). The six possible paths between each illness perception and depressive symptom scores at the two time points were tested by conducting six hierarchical linear regressions with bias-accelerated bootstrap (1000 samples). Causal inference was determined by examining which of the two cross-lagged coefficients was larger. If the cross-lagged coefficients were equal, this indicated that the variables were caused by another variable or were mutually influencing each other (Watkins & Styck, 2017).

Figure 1.

Two-wave cross-lagged panel design



3. Results

3.1 Preliminary Analyses

Mann-Whitney U tests were conducted to investigate any baseline differences between the 27 participants that were excluded and the 135 that were included. The majority of baseline measures of those who were included did not differ significantly from the participants that were dropped from the study. Illness perceptions about identity differed significantly between the excluded (*Mdn* = 9) and included (*Mdn* = 7) participants, $U = 1309.50$, $z = -2.34$, $p < .05$, $r = -.18$. Pain severity was also significantly different between the excluded (*Mdn* = 62) and included (*Mdn* = 41) participants, $U = 1293.50$, $z = -2.38$, $p < .05$, $r = -.019$.

Prior to the main analyses data screening was conducted to inspect assumptions of normality and outliers. Histograms, P-plots, *z* scores of skewness and kurtosis and Kolmogorov-Smirnov tests were used to check for normality. Baseline and follow-up DLQI, GAD-2 and PHQ-2 ranged from 0.11 to 4.22 and -2.46 to 0.01 for skewness and kurtosis respectively. This exceeded lower (1.96) and upper thresholds (3.29) of normality (Field, 2009). Baseline and follow-up illness perceptions also ranged from -

8.64 to -1.12 and -2.18 to 6.45 for skewness and kurtosis, respectively. Kolmogorov-Smirnov tests also indicated that data on DLQI, GAD-2, PHQ-2 and illness perceptions all significantly differed from normality. Boxplots were then inspected for possible outliers. None were detected for DLQI, GAD-2 and PHQ-2 scores, however boxplots of illness perceptions including baseline consequences, concern and timeline and follow-up timeline and identity indicated possible outliers. Five of the outlying cases across these variables had an asterisk indicating that they are extreme outliers, and were checked for data entry errors, however no errors were identified. All analyses for the hypothesis were re-run with these five cases removed, however there were no changes to the results in terms of overall significance of the regression models and they were therefore retained in the study. In light of these preliminary analyses and assumptions of normality being violated non-parametric tests were run to analyse relationships between illness perceptions and outcomes.

Multiple Regression Preliminary Analysis

Three multiple linear regressions were conducted to assess the ability of baseline demographics, disease severity and illness perceptions to predict quality of life and symptoms of anxiety and depression at follow-up. Initially, baseline outcomes measures were included as predictors in these regressions in order to control for the effect of these variables. Since it was expected that the values of these baseline outcome measures would dominate the prediction models, an additional three multiple linear regressions were conducted to compare findings without baseline outcome measures included. Residual statistics of the regression models and examination of the histograms and scatterplots of standardised residuals of outcomes indicated that further inspection was required of possible outliers. Cook's distance, average leverage, Mahalanobis distance, standardised DFBeta and covariance ratios (CVR) were analysed for each regression. Cook's distance and standardised DFBeta estimates were assessed in relation to the threshold of > 1, and average leverage in relation to the value of > 0.24 (2(k + 1) / n) and > 0.35 (3(k + 1) / n), (Cook & Weisberg, 1982; Field, 2009; Hoaglin & Welsch, 1978; Stevens, 2002). Mahalanobis distance estimates were checked with the cut off of > 20 and CVRs falling outside of the range of 0.65 - 1.35 (1 - (3(k + 1) / n and 1+ (3(k + 1) / n) were inspected (Barnett & Lewis, 1978; Belsey, Kuh & Welsch, 1980). To correct for outliers, heteroscedasticity and other influential areas found across the regressions, bias-

accelerated (BCA) bootstrapping (1000 samples) was used (Efron, 1987; Frangos & Schucany, 1990; Hall, 1988).

Inspection of residual statistics for the multiple regression of DLQI (with baseline DLQI included as a predictor) indicated that two cases were above the recommended cut-off of > 2.5 (one was > 3). Visual inspection of scatterplots indicated one case as a potential outlier. Following closer inspection these cases met all criteria stated above, apart from two having CVRs slightly below threshold and one above threshold. The regression was re-run with these cases excluded to investigate impact on findings, however overall significance of variance explained by the models remained the same (pain severity became a significant predictor in models one and two).

For the multiple regression of DLQI without baseline DLQI included as a predictor, one of the same cases had a residual statistic above 3 and the same potential outlier was found on the scatterplot. On closer inspection this case met all criteria stated above apart from a similarly high CVR above threshold on one case. The regression was re-run without these cases to investigate influence on findings. The overall significance of findings remained the same, however illness perceptions about consequences, treatment control, identity and emotional response became significant predictors).

The multiple regression of GAD-2 with baseline GAD-2 included as a predictor also indicated two cases with residual statistics above 2.5, and the scatterplot indicated one case as a potential outlier. On closer inspection these cases met all criteria stated above, apart from two cases falling slightly below CVR threshold. After re-running the regression without these cases overall findings remained the same. For the multiple regression of GAD-2 without baseline GAD-2, two potential outliers were identified on the scatterplots, however on closer inspection these cases met all criteria stated above apart from one case with a slightly low CVR. When this regression was re-run with these cases removed there was no overall change, apart from gender and illness perceptions about consequences becoming significant predictors in model 3.

There was one case with a residual statistic above 2.5 in the multiple regressions of PHQ-2 with and without baseline PHQ-2 included as a predictor, which is reasonable to expect within a sample of this size. Two potential outliers were identified on the

scatterplot of PHQ-2 scores with baseline PHQ-2 included. On closer inspection these cases met all criteria stated above, apart from one which had a CVR slightly below threshold. When these cases were removed from the regression including baseline PHQ-2, change in variance explained from model one to model two (HS severity) became statistically significant, and in model three age and higher Hurley stages at baseline became significant predictors of PHQ-2 at follow-up. For the regression without PHQ-2 baseline included the case with the residual statistic above 2.5 was removed, and variance explained by the models did not change significantly, however a higher Hurley stage at baseline became a significant predictor in models one and two.

3.2 Demographic and Clinical Characteristics

There was a total of 135 participants with HS aged 18-63 (M = 38.90, SD = 11.48) at baseline, and 19 - 63 (M = 39.62, SD = 11.39) at follow-up. The majority of participants were female (n = 79, 59%), had severe HS at both time points (T1 = 56%, T2 = 54%) followed by moderate HS (T1 = 30%, T2 = 26%), and mild HS (T1 = 15%, T2 = 20%) respectively. Pain severity scores ranged from 0-96 at baseline (M = 42.47, SD = 28.94), and 0 - 100 at follow-up (M = 40.99, SD = 30.07). The average duration between baseline and follow-up was 8.83 months (SD = 2.79, $Mode$ = 5.98) ranging from 5.98 - 20.47 months. Table 1 displays the demographic and clinical characteristics of the participants.

3.3 Illness Perceptions

The distribution of illness perception scores at baseline and follow-up, and the number and percentage of people who were above the mid-point of > 5 for each perception are shown in Table 2. At both time 1 and time 2, the highest numbers of participants scoring above mid-point were for illness perceptions about timeline (86% and 85% respectively) and concern about HS (86% and 72% respectively). This indicates that the majority of participants perceived HS as having a long timeline and were greatly concerned about HS. Over two thirds of participants rated at baseline and follow-up that HS has a strong impact on their life (consequences), they have high amounts of symptoms (identity) and that HS has a strong emotional impact on them. Over half of the participants also felt that they have low control over their illness at both time points. Most participants felt they had a good understanding of their HS and perceived treatment for HS as fairly helpful. Numbers of participants scoring above mid-point reduced from baseline to follow-up for all illness perceptions.

Table 1.

Demographic and Clinical Characteristics at Baseline and Follow-up

	Baseline (T1)	**Follow-up (T2)**
Characteristic	***n* (%)**	***n* (%)**
Gender		
Female	79 (59%)	79 (59%)
Male	56 (42%)	56 (42%)
Age (years)		
Mean (*SD*)	38.90 (11.48)	39.62 (11.39)
Range	18 - 63	19 - 63
Hurley stage of HS severity		
Stage I and I/II (Mild)	20 (15%)	27 (20%)
Stages II and II/III (Moderate)	40 (30%)	35 (26%)
Stage III (Severe)	75 (56%)	73 (54%)
Pain severity		
Mean (*SD*)	42.47 (28.94)	40.99 (30.07)
Range	0 - 96	0 - 100

3.4 Symptoms of Anxiety and Depression and Quality of Life

Table 3 illustrates the distribution of anxiety and depression symptom scores, and the number and percentage of participants that were equal to or above the cut-off for clinically significant symptoms. At both time one and time two, participants typically scored below threshold for clinically significant symptoms of anxiety (T1: *Mdn* = 2, *SD* = 1.85; T2: *Mdn* = 2, *SD* = 1.78) and depression (T1: *Mdn* = 2, *SD* = 1.79; T2: *Mdn* = 2, *SD* = 1.93). Less than a third of participants scored above the cut-off for anxiety symptoms at both time points (28% and 27% respectively). Over a third of participants met threshold for clinically significant depressive symptoms at baseline (35%), however this reduced to just under a third at follow-up (32%).

Table 2.

Illness Perception (BIPQ) Scores and Participants Numbers Above Mid-Point at Baseline and Follow-Up

	Baseline (T1)			Follow-up (T2)		
Dimension	**Mean* (*SD*)**	**Median**	**BIPQ score above mid-point (> 5) *n* (%)**	**Mean* (*SD*)**	**Median**	**BIPQ score above mid-point (> 5) *n* (%)**
Consequences	7.02 (2.53)	7	104 (77%)	6.70 (2.74)	7	90 (68%)
Timeline	8.56 (2.43)	10	116 (86%)	8.56 (2.40)	10	114 (85%)
Personal control	2.98 (3.02)	2	96 (71%)	3.29 (2.93)	3	83 (62%)
Treatment control	5.52 (3.00)	5	44 (33%)	5.72 (2.84)	5	38 (28%)
Identity	7.10 (2.40)	7	101 (75%)	6.61 (2.41)	7	94 (70%)
Concern	8.11 (2.24)	9	116 (86%)	7.38 (2.93)	8	97 (72%)
Understanding	7.23 (2.64)	8	18 (13%)	7.67 (2.58)	8	16 (12%)
Emotional response	7.33 (2.96)	8	106 (79%)	7.08 (2.69)	8	95 (70%)

*Higher scores indicate stronger endorsement of items. The number and percent of BIPQ scores above mid-point for personal control, treatment control and understanding are calculated using reverse scoring.

Overall, participants rated that HS symptoms were having a very large impact (Hongbo et al., 2005) on QoL at baseline (DLQI *Mdn* = 15, *SD* = 8.22) and follow-up (DLQI *Mdn* = 13, *SD* = 8.13). Table 4 displays the distribution of DLQI scores in at each level of impact on QoL. Over a third of participants gave a score falling in the very large impact range on the DLQI at time 1 (35%) and 2 (39%) and almost a third scored symptoms as having an extremely large impact (31% and 24% respectively). Less than 5% of participants reported HS as having no effect on their quality of life.

Table 3.

Total Scores of Anxiety (GAD-2) and Depression (PHQ-2) Symptom, and Participant Numbers Reaching Threshold for Clinically Significant Symptoms at Baseline and Follow-Up

	Baseline (T1)			Follow-up (T2)		
Outcome	**Mean (*SD*)**	**Median**	**Participants scoring above threshold for clinically significant symptoms (≥ 3) *n* (%)**	**Mean (*SD*)**	**Median**	**Participants scoring above threshold for clinically significant symptoms (≥ 3) *n* (%)**
GAD-2	1.93 (1.85)	2	37 (28%)	1.77 (1.78)	2	36 (27%)
PHQ-2	2.22 (1.79)	2	47 (35%)	2.04 (1.93)	2	43 (32%)

Table 4.

Total Scores of the Impact of HS on Quality of Life (DLQI) at Baseline and Follow-Up

	DLQI category				
Time point	**No effect on QoL *n* (%)**	**Small effect on QoL *n* (%)**	**Moderate effect on QoL *n* (%)**	**Very large effect on QoL *n* (%)**	**Extremely large effect on QoL *n* (%)**
Baseline (T1)	5 (4%)	14 (10%)	27 (20%)	47 (35%)	42 (31%)
Follow-up (T2)	4 (3%)	21 (16%)	26 (19%)	52 (39%)	32 24%)

3.5 Relationships Between Factors at Baseline and Quality of Life and Symptoms of Anxiety and Depression at Follow-Up

Hypothesis: Illness beliefs assessed at first presentation to the clinic will be a stronger predictor of longitudinal outcomes (quality of life and symptoms of anxiety and depression) than HS disease severity.

Tables 5, 7 and 9 display the multiple regressions with baseline outcome measures included as predictors, and Tables 6, 8 and 10 display the multiple regressions without baseline outcome measures included.

Anxiety

For anxiety symptom scores at follow-up, Table 5 demonstrates that when baseline anxiety symptoms were included in the model, HS severity (Hurley stage) did not explain a significant amount of additional variance over and above demographics, pain severity and baseline anxiety ($\Delta R^2 = .015$, $\Delta F(2, 128) = 1.35$, $p = .263$). When illness perceptions were added into the model this produced a larger increase in variance explained (4.7%), however this was not statistically significant ($\Delta R^2 = .047$, $\Delta F(8, 120) = 1.07$, $p = .386$). Standardised beta coefficients indicated that baseline anxiety scores remained a significant contributor to the model after Hurley stage and illness perceptions were entered ($\beta = .37$, $p < .01$, 95% *CI* [0.11, 0.60]). Greater emotional response to HS at baseline also explained a significant amount of variance in anxiety symptoms at follow-up ($\beta = .18$, $p < .05$, 95% *CI* [-0.02, 0.23]).

Table 6 demonstrates the same model with baseline anxiety symptoms removed. HS severity (Hurley stage) still did not significantly increase the amount of variance explained over and above demographic variables and pain severity ($\Delta R^2 = .017$, $\Delta F(2, 129) = 1.24$, $p = .293$). Illness perceptions made the largest contribution to the model explaining a statistically significant increase in variance (13.7%) in anxiety symptoms at follow-up ($\Delta R^2 = .137$, $\Delta F(8, 121) = 2.79$, $p < .01$), with baseline emotional response remaining a significant contributor to this model ($\beta = .30$, $p <. 01$, 95% *CI* [0.05, 0.30]). Standardised beta coefficients also indicated that pain severity at baseline explained a significant amount of variance in anxiety scores at follow-up when Hurley stage was included in the model ($\beta = .30$, $p < .01$, 95% *CI* [0.01, 0.03]) however this was no longer significant when illness perceptions had been accounted for ($\beta = .09$, $p = .459$, 95% *CI* [-0.01, 0.02]). These findings from Tables 5 and 6 support hypothesis 1 that illness beliefs were a stronger predictor of anxiety at follow-up than disease severity.

Table 5.

Hierarchical Multiple Regressions of Variables on Anxiety (GAD-2) Symptoms at Time 2

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	-.06	0.26	.463 (-0.73, 0.27)	-.08	0.28	.340 (-0.81, 0.21)	-.10	0.30	.271 (-0.95, 0.24)
Age	-.01	0.01	.923 (-0.02, 0.02)	.035	0.01	.653 (-0.02, 0.03)	.09	0.01	.305 (-0.01, 0.04)
GAD-2 total	**.46**	**0.10**	**.001 (0.22, 0.65)**	**.46**	**0.10**	**.001 (0.23, 0.65)**	**.37**	**0.11**	**.004 (0.11, 0.60)**
Pain	.13	0.01	.214 (-0.00, 0.02)	.15	0.01	.163 (-0.00, 0.02)	.04	0.01	.735 (-0.01, 0.02)
Lower Hurley stage (I vs. II)				-.08	0.47	.520 (-1.23, 0.47)	-.06	0.48	.646 (-1.08, 0.59)
Higher Hurley stage (I vs. III)				-.18	0.44	.155 (-1.50, 0.15)	-.16	0.46	.230 (-1.43, 0.23)
Consequences							.09	0.10	.514 (-0.13, 0.27)
Timeline							-.06	0.09	.631 (-0.18, 0.13)
Personal control							-.05	0.04	.511 (-0.11, 0.07)
Treatment control							-.05	0.05	.581 (-0.13, 0.08)
Identity							.06	0.08	.569 (-0.13, 0.18)
Concern							-.03	0.08	.729 (-0.18, 0.13)
Understanding							.04	0.06	.660 (-0.09, 0.14)
Emotional response							**.18**	**0.06**	**.048 (-0.02, 0.23)**
R^2		.282			.297			.344	
ΔR^2 *(P)*		**.282 (.000)**			.015 (.263)			.047 (.386)	

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values and 95% *CIs* are bootstrapped (1000 samples).

Table 6.

Hierarchical Multiple Regressions of Variables on Anxiety (GAD-2) Symptoms at Time 2 Without GAD-2 at Baseline

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	-.11	0.29	.180 (-1.00, 0.20)	-.13	0.30	.131 (-1.19, 0.20)	-.15	0.31	.074 (-1.18, 0.11)
Age	-.08	0.01	.423 (-0.04, 0.02)	-.03	0.01	.745 (-0.03, 0.02)	.09	0.02	.370 (-0.02, 0.05)
Pain	**.28**	**0.01**	**.006 (0.00, 0.03)**	**.30**	**0.01**	**.005 (0.01, 0.03)**	.09	0.01	.459 (-0.01, 0.02)
Lower Hurley stage (I vs. II)				-.06	0.52	.667 (-1.18, 0.73)	-.03	0.50	.800 (-1.08, 0.79)
Higher Hurley stage (I vs. III)				-.18	0.49	.198 (-1.60, 0.44)	-.15	0.48	.259 (-1.44, 0.45)
Consequences							.20	0.09	.097 (-0.03, 0.33)
Timeline							-.08	0.08	.434 (-0.18, 0.09)
Personal control							.01	0.05	.940 (-0.08, 0.11)
Treatment control							-.10	0.05	.198 (-0.16, 0.03)
Identity							.05	0.09	.690 (-0.15, 0.20)
Concern							-.09	0.08	.372 (-0.23, 0.08)
Understanding							.01	0.06	.884 (-0.10, 0.12)
Emotional response							**.30**	**0.05**	**.001 (0.05, 0.30)**
R^2			.102			.119			.256
ΔR^2 *(P)*			**.102 (.003)**			.017 (.293)			**.137 (.007)**

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values, and 95% *CI*s are bootstrapped (1000 samples).

Depression

For symptoms of depression, Table 7 indicates that when baseline depression symptoms are included in the model, Hurley stage did not explain a significant amount of additional variance over and above that explained by baseline demographics, pain severity and depression scores ($\Delta R^2 = 0.034$, $\Delta F(2, 128) = 2.90$, $p = .059$), however it did reach borderline statistical significance. Baseline illness perceptions also did not explain a significant amount of additional variance in depression symptom scores at follow-up ($\Delta R^2 = .063$, $\Delta F(8, 120) = 1.39$, $p = .208$). The standardised beta coefficients show that baseline depression scores ($\beta = .31$, $p < .01$, 95% *CI* [0.14, 0.54]) and pain severity ($\beta = .28$, $p < .01$, 95% *CI* [0.01, 0.03]) remain significant contributors until illness perceptions are added to the model. Higher Hurley stage at baseline was a significant contributor to depression scores at follow-up when illness perceptions were not accounted for ($\beta = -.26$, $p < .05$, 95% *CI* [-1.96, -0.13]), however this reduced to borderline significance when illness perceptions were entered ($\beta = .23$, $p = .052$, 95% *CI* [-1.84, 0.01]). Similar to findings with anxiety, greater emotional response to HS explained a significant amount of variance in depression symptom scores at follow-up ($\beta = .21$, $p < .05$, 95% *CI* [-0.01, 0.26]).

Table 8 displays the same model with baseline depression symptom scores removed. Entry of baseline Hurley stage into the model only explained an additional 2.5% of the variance which was not a statistically significant increase from that explained by demographics and pain severity ($\Delta R^2 = .025$, $\Delta F(2, 129) = 1.94$, $p = .147$). Illness perceptions at baseline explained an additional 11.2% of the variance which was a significant increment ($\Delta R^2 = .112$, $\Delta F(8, 121) = 2.41$, $p < .05$), with emotional response to HS having the greatest impact on the model ($\beta = .22$, $p < .05$, 95% *CI* [0.01, 0.26]. Pain severity also remained a significant contributor to the model when Hurley stage was accounted for, however this became non-significant when illness perceptions were added ($\beta = .21$, $p = .091$, 95% *CI* [-0.00, 0.03]). These findings from Tables 7 and 8 support the hypothesis that illness beliefs were a stronger predictor of symptoms of depression at follow-up than HS disease severity.

Table 7.

Hierarchical Multiple Regressions of Variables on Depression (PHQ-2) Symptoms at Time 2

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	.01	0.31	.931 (-0.58, 0.61)	-.02	0.31	.814 (-0.66, 0.48)	-.03	0.35	.739 (-0.83, 0.58)
Age	-.01	0.01	.900 (-0.03, 0.02)	.06	0.01	.503 (-0.02, 0.03)	.14	0.01	.076 (-0.00, 0.05)
PHQ-2 total	**.29**	**0.11**	**.007 (0.11, 0.50)**	**.31**	**0.11**	**.006 (0.14, 0.52)**	.21	0.12	.061 (-0.02, 0.45)
Pain	**.27**	**0.01**	**.013 (0.00, 0.03)**	**.28**	**0.01**	**.009 (0.01, 0.03)**	.16	0.01	.180 (-0.01, 0.03)
Lower Hurley stage (I vs. II)				-.11	0.50	.357 (-1.45, 0.51)	-.09	0.50	.460 (-1.32, 0.61)
Higher Hurley stage (I vs. III)				**-.26**	**0.44**	**.024 (-1.96, -0.13)**	-.23	0.45	.052 (-1.84, 0.01)
Consequences							.13	0.10	.314 (-0.09, 0.33)
Timeline							-.10	0.07	.264 (-0.22, 0.08)
Personal control							.01	0.06	.872 (-0.11, 0.14)
Treatment control							-.03	0.06	.745 (-0.14, 0.12)
Identity							.09	0.10	.465 (-0.12, 0.25)
Concern							-.02	0.09	.797 (-0.20, 0.16)
Understanding							-.01	0.06	.879 (-0.13, 0.09)
Emotional response							**.21**	**0.07**	**.029 (-0.01, 0.26)**
R^2			.225			.258			.321
ΔR^2 *(P)*			**.225 (.000)**			.034 (.059)			.063 (.208)

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Table 8.

Hierarchical Multiple Regressions of Variables on Depression (PHQ-2) Symptoms at Time 2 Without PHQ-2 at Baseline

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	-.04	0.32	.649 (-0.76, 0.48)	-.06	0.32	.440 (-0.87, 0.37)	-.07	0.33	.426 (-0.90, 0.37)
Age	-.02	0.01	.848 (-0.03, 0.03)	.04	0.02	.669 (-0.02, 0.04)	.15	0.01	.078 (-0.00, 0.05)
Pain	**.40**	**0.01**	**.001 (0.02, 0.04)**	**.42**	**0.01**	**.001 (0.02, 0.04)**	.21	0.01	.091 (-0.00, 0.03)
Lower Hurley stage (I vs. II)				-.11	0.53	.376 (-1.55, 0.57)	-.10	0.50	.431 (-1.33, 0.57)
Higher Hurley stage (I vs. III)				-.23	0.49	.069 (-1.87, 0.18)	-.22	0.48	.088 (-1.78, 0.17)
Consequences							.21	0.09	.079 (0.00, 0.35)
Timeline							-.08	0.07	.360 (-0.19, 0.08)
Personal control							.03	0.06	.805 (-0.10, 0.15)
Treatment control							-.09	0.06	.285 (-0.17, 0.06)
Identity							.08	0.10	.506 (-0.12, 0.23)
Concern							-.02	0.09	.824 (-0.19, 0.15)
Understanding							-.01	0.07	.922 (-0.14, 0.11)
Emotional response							**.22**	**0.07**	**.035 (0.01, 0.28)**
R^2			.161			.186			.298
ΔR^2 *(P)*			**.161 (.000)**			.025 (.147)			**.112 (.019)**

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Quality of Life

For QoL, Table 9 demonstrates that when baseline QoL scores were included in the model in addition to demographics and pain severity, Hurley stage ($\Delta R^2 = .003$, $\Delta F(2, 128) = .377$, $p = .686$) and illness perceptions ($\Delta R^2 = .016$, $\Delta F(8, 120) = .481$, $p = .868$) at baseline did not significantly increase the variance explained for scores of QoL at follow-up. Baseline QoL explained the most variance in QoL at follow-up when all variables were entered into the model ($\beta = .50$, $p < .01$, 95% *CI* [0.26, 0.73]).

When baseline QoL was removed as a predictor (Table 10), Hurley stage only explained an additional 1.1% of the variance for QoL at follow-up ($\Delta R^2 = .011$, $\Delta F(2, 129) = .965$, $p = .384$), whereas illness perceptions explained an additional 12.1% of the variance ($\Delta R^2 = .121$, $\Delta F(8, 121) = 3.09$, $p < .01$). Pain severity at baseline made a consistently significant contribution to the model with all other variables accounted for ($\beta = .28$, $p < .01$, 95% *CI* [-0.02, 0.13]). Greater experiences of HS symptoms (Identity) was also a significant contributor to QoL at follow-up ($\beta = .21$, $p < .05$, 95% *CI* [-0.02, 1.48]). Overall these findings support the hypothesis that illness perceptions are a stronger predictor of quality of life impairment than disease severity in HS.

3.6 Stability of illness perceptions over time

Table 11 demonstrates that Friedman's two-way analysis of variance by ranks revealed that illness perceptions did not significantly change between baseline and follow-up, apart from Identity ($X^2(1) = 7.84$, $p < .05$ and Concern ($X^2(1) = 9.00$, $p < .05$). Wilcoxon signed-rank tests were conducted to follow-up these findings. A Bonferroni correction was used therefore a .0167 level of significance was applied to all effects. It appeared that perceptions about Identity ($Mdn = 2$, $T = 1706.00$, $z = -2.842$, $p < .05$, $r = -.17$) and Concern ($Mdn = 1$, $T = 984.50$, $z = -3.204$, $p < .05$, $r = -.20$) were not stable over time; scores for these illness perceptions were lower at follow-up compared to baseline.

Table 9.

Hierarchical Multiple Regressions of Variables on Quality of Life (DLQI) at Time 2

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	-.06	1.07	.338 (-3.11, 1.01)	-.07	1.13	.341 (-3.43, 1.11)	-.06	1.25	.440 (-3.33, 1.38)
Age	.06	0.05	.344 (-0.05, 0.14)	.07	0.05	.310 (-0.05, 0.15)	.10	0.05	.182 (-0.03, 0.18)
DLQI total	**.59**	**0.08**	**.001 (0.43, 0.72)**	**.59**	**0.08**	**.001 (0.42, 0.75)**	**.50**	**0.11**	**.001 (0.26, 0.73)**
Pain	.14	0.02	.092 (-0.01, 0.09)	.14	0.02	.096 (-0.01, 0.09)	.11	0.03	.276 (-0.02, 0.09)
Lower Hurley stage (I vs. II)				-.08	1.83	.439 (-5.08, 2.31)	-.07	1.85	.478 (-4.72, 2.16)
Higher Hurley stage (I vs. III)				-.07	1.71	.531 (-4.25, 2.29)	-.04	1.81	.734 (-4.10, 2.76)
Consequences							-.01	0.37	.911 (-0.81, 0.70)
Timeline							-.02	0.22	.759 (-0.50, 0.40)
Personal control							.06	0.17	.311 (-0.17, 0.49)
Treatment control							-.04	0.20	.592 (-0.47, 0.33)
Identity							.12	0.35	.245 (-0.29, 1.05)
Concern							.03	0.36	.768 (-0.63, 0.71)
Understanding							-.04	0.22	.589 (-0.54, 0.25)
Emotional response							.09	0.31	.429 (-0.41, 0.82)
R^2			.474			.477			.494
ΔR^2 *(P)*			**.474 (.000)**			.003 (.686)			.016 (.868)

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Table 10.

Hierarchical Multiple Regressions of Variables on Quality of Life (DLQI) at Time 2 Without DLQI at Baseline

	Model 1			**Model 2**			**Model 3**		
Variables at T1	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**	**β**	***SE***	***P* (95% *CI*)**
Gender	-.10	1.24	.187 (-4.05, 0.65)	-.09	1.26	.256 (-3.91, 1.11)	-.08	1.29	.346 (-3.91, 1.50)
Age	.02	0.06	.816 (-0.10, 0.13)	-.01	0.06	.920 (-0.12, 0.14)	.10	0.06	.221 (-0.03, 0.18)
Pain	**.52**	**0.02**	**.001 (0.10, 0.19)**	**.51**	**0.02**	**.001 (0.09, 0.19)**	**.28**	**0.03**	**.008 (0.02, 0.13)**
Lower Hurley stage (I vs. II)				-.06	1.98	.599 (-4.76, 3.27)	-.04	1.86	.701 (-4.34, 3.31)
Higher Hurley stage (I vs. III)				.06	1.89	.587 (-2.27, 4.89)	.08	1.77	.484 (-2.04, 4.68)
Consequences							.12	0.37	.287 (-0.39, 1.15)
Timeline							-.05	0.25	.489 (-0.66, 0.48)
Personal control							.10	0.19	.166 (-0.48, 0.63)
Treatment control							-.10	0.19	.162 (-0.64, 0.06)
Identity							**.21**	**0.33**	**.035 (-0.02, 1.48)**
Concern							.00	0.40	.980 (-0.84, 0.75)
Understanding							-.11	0.22	.123 (-0.74, 0.04)
Emotional response							.19	0.31	.086 (-0.18, 1.04)
R^2			.278			.288			.409
ΔR^2 *(P)*			**.278 (.000)**			.011 (.384)			**.121 (.003)**

Note. β = standardised coefficient. ΔR^2 = change in R^2. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Table 11.

Summary of Friedman's Two-Way Analysis of Variance by Ranks and Wilcoxon Signed-Ranks Test Statistics Assessing Change in Illness Perceptions Between Baseline and Follow-Up

Illness perception	Friedman test statistic of change between T1 and T2 (X^2)	*P* value	Wilcoxon signed-rank test statistic of change between T1 and T2 (*T*)	Bonferroni correction *P* value
Consequences	3.18	.075	-	-
Timeline	0.02	.895	-	-
Personal control	0.25	.615	-	-
Treatment control	0.09	.765	-	-
Identity	**7.84**	**.005***	**1706.00**	**.004****
Concern	**9.00**	**.003***	**984.50**	**.001****
Understanding	1.36	.244	-	-
Emotional response	2.71	.100	-	-

*$p < .01$ (2-tailed), **$p < .0167$ (2-tailed).

Table 12.

Spearman's Rho Correlation Coefficients Between Change Scores in Illness Perceptions Over Time and Quality of Life (DLQI) and Symptoms of Anxiety (GAD-2) and Depression (PHQ-2) at Follow-Up

	Outcome (T2)		
Illness perception	**GAD-2**	**PHQ-2**	**DLQI**
Consequences	.091	.082	**.244****
Timeline	.076	**.182***	**.192***
Personal control	-.073	**-.185***	-.169
Treatment control	.073	.037	.010
Identity	.038	.123	.101
Concern	**.316****	.132	**.241****
Understanding	-.004	.038	-.039
Emotional response	.094	.068	.168

*$p < .05$ (2-tailed), **$p < .01$ (2-tailed).

Relationships Between Changes in Illness Perceptions Over Time and Symptoms of Anxiety and Depression and Quality of Life

Spearman's rho correlation coefficients in Table 12 show that there was a significant positive relationship between the DLQI total score at follow-up and change in illness perceptions about consequences (r_s = .244, p < .01), timeline (r_s = .192, p < .05), and concern (r_s = .241, p < .01). Personal control (r_s = -.169, p = .05) and emotional response (r_s = .168, p = .051) were on the borderline of statistical significance for negative and positive relationships, respectively with DLQI total score. Changes in illness perceptions were not significantly related to the GAD-2 total score at follow-up, apart from reductions in illness perceptions about concern (r_s = .316, p < .001) which were associated with lower GAD-2 scores. Changes in illness perceptions were not significantly related to the PHQ-2 total score at follow-up, apart from a positive correlation with change in illness perceptions about timeline (r_s = .182, p < .05) and a negative correlation with change in personal control (r_s = -.185, p < .05). In contrast to anxiety and quality of life, increases in understanding over time were associated with higher PHQ-2 scores at follow-up.

3.7 Cross-Lagged Panel Analysis of Illness Perceptions and Symptoms of Depression Over Time

Spearman's rho analyses were run prior to cross-lagged analyses to identify illness perceptions that correlated with symptoms of depression at the level of .3 or over. Consequences, personal control, identity, concern and emotional response met this criterion and all other illness perceptions were excluded from this part of the analyses.

Figure 2 demonstrates the standardised regression coefficients for each pathway between illness beliefs about consequences of HS and symptoms of depression over time (see Table 13 for further details of each regression). All paths were statistically significant at $p \leq .001$. Symptoms of depression and beliefs about consequences of HS showed a similar pattern of stability over time (.41 and .55 respectively) and the synchronous paths (associations at the same time point) had similar effect sizes in both directions at each time point, as shown in Table 13 (.54 and .47, respectively). Both significant cross-lagged paths indicate that more negative beliefs about the consequences of HS predict higher scores of depression symptoms over time (β = .42, $p \leq .001$, 95% *CI* [0.21, 0.43]) and

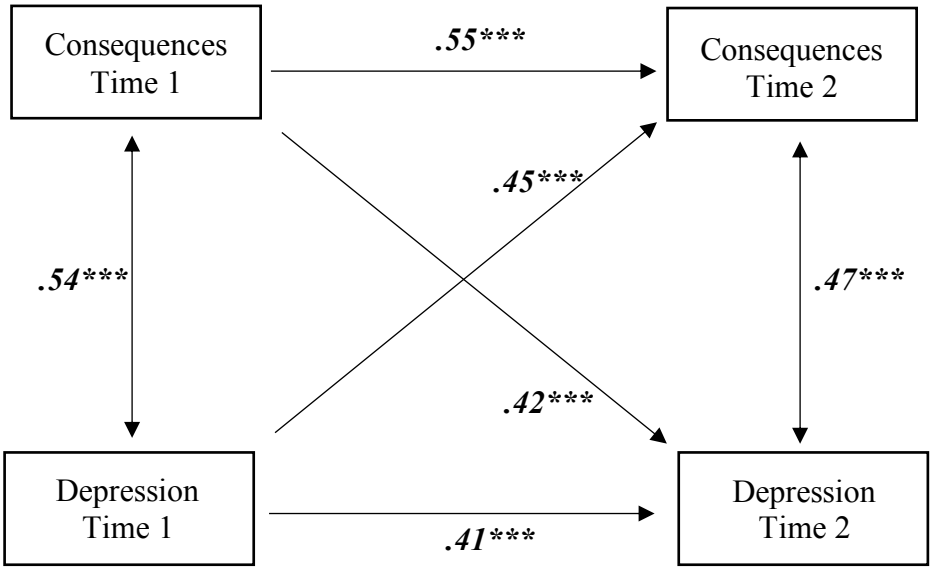
higher scores of depression symptoms predict more negative beliefs about consequences over time (β = .45, $p \leq .001$, 95% *CI* [0.45, 0.94]). The similar effect sizes and level of significance for all paths indicate that symptoms of depression and beliefs about consequences of HS had a mutual influence on each other regardless of time. Although the directions of influence were mutual, the influence of depression symptoms and beliefs about consequences on each other at baseline was slightly larger than over time, as shown by the lower effect sizes of the cross-lagged paths.

The standardised regression coefficients for each pathway between illness beliefs about personal control over HS and symptoms of depression over time are displayed in Figure 3 (see Table 14 for further details). Personal control beliefs at baseline were significantly associated with these beliefs at follow-up, even though the pattern was the least stable of the illness perceptions measures. Synchronously, effect sizes were negatively associated and similar in both directions at each time point (as shown in Table 14), however the synchronous coefficients changed from non-significant to significant over time (-.12 and -.31, respectively). The cross-lagged effect of depression symptoms on personal control was significant (β = -.20, $p < .05$, 95% *CI* [-0.58, 0.06]), whereas the impact of personal control on depression symptoms over time was non-significant (β = -.14, $p = .104$, *ns*, 95% *CI* [-0.20, 0.02]). These negative cross-lagged paths suggest that higher scores of depression symptoms only predicted lower personal control scores at a later time not at the same time point (baseline). Personal control beliefs did not predict depression symptoms at baseline or follow-up. This suggests that depressive symptoms had more of an impact over time than personal control beliefs.

Figure 4 shows the standardised regression coefficients for the pathways between identity beliefs and depressive symptoms over time (see Table 15 for further details). All paths were statistically significant at $p \leq .001$. The synchronous paths had similar effect sizes in both directions at each time point (.37 and .43). The trend of similarity in both cross-lagged paths suggests that identity beliefs and symptoms of depression had a mutual influence on each other from baseline to follow-up. Higher identity beliefs at baseline predicted higher scores of depression symptoms (β = .35, $p \leq .001$, 95% *CI* [0.16, 0.42]), and higher scores of depressive symptoms at baseline predicted higher identity beliefs over time (β = .35, $p \leq .001$, 95% *CI* [0.24, 0.69]).

Figure 2.

Standardised Regression Coefficients (β) in a Cross-Lagged Panel Model Demonstrating the Effect of Illness Beliefs About the Consequences of HS on Symptoms of Depression, and the Effect of Depressive Symptoms on Beliefs About Consequences of HS Over Time



Note. P values are bootstrapped (1000 samples).

*Coefficient is significant at $p < .05$, **coefficient is significant at $p < .01$, ***coefficient is significant at $p \leq .001$.

Table 13.

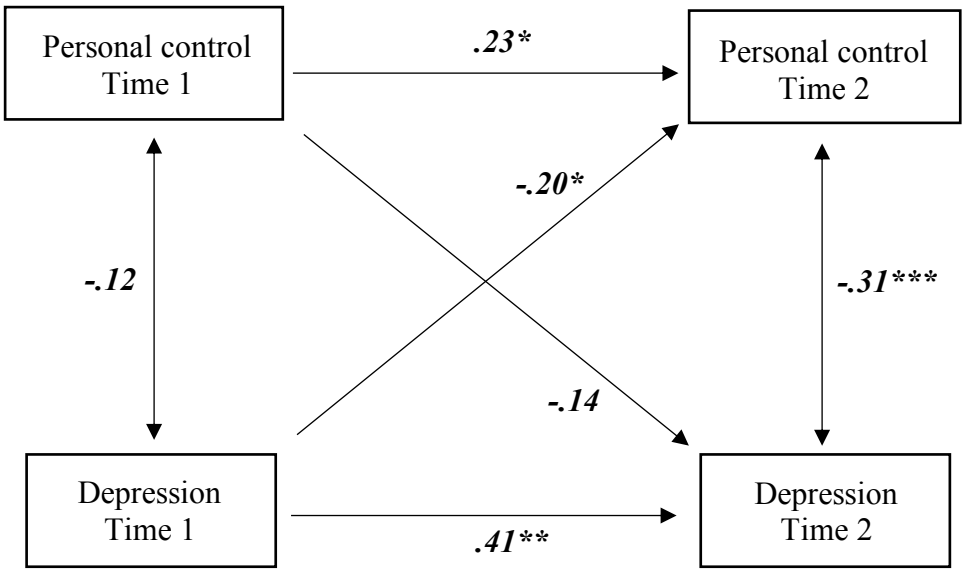
Linear Regression Analyses Explaining the Cross-Lagged Panel Model of Illness Beliefs About the Consequences of HS and Symptoms of Depression

Linear regression pathways	**β**	***SE***	***P* (95% *CI*)**
Consequences T1 -> Consequences T2	.55	.08	.001 (0.42, 0.75)
PHQ-2 T1 -> PHQ-2 T2	.41	.09	.001 (0.27, 0.61)
Consequences T1 -> PHQ-2 T1	.54	.05	.001 (0.28, 0.48)
PHQ-2 T1 -> Consequences T1	.54	.10	.001 (0.56, 0.96)
Consequences T2 -> PHQ-2 T2	.47	.05	.001 (0.23, 0.43)
PHQ-2 T2 -> Consequences T2	.47	.11	.001 (0.45, 0.89)
Consequences T1 -> PHQ-2 T2	.42	.05	.001 (0.21, .0.43)
PHQ-2 T1 -> Consequences T2	.45	.11	.001 (0.45, 0.94)

Note. β = standardised coefficient. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Figure 3.

Standardised Regression Coefficients (β) in a Cross-Lagged Panel Model Demonstrating the Effect of Illness Beliefs About Personal Control Over HS on Symptoms of Depression, and the Effect of Depressive Symptoms on Beliefs About Personal Control Over Time



Note. P values are bootstrapped (1000 samples).

*Coefficient is significant at $p < .05$, **coefficient is significant at $p < .01$, ***coefficient is significant at $p \leq .001$.

Table 14.

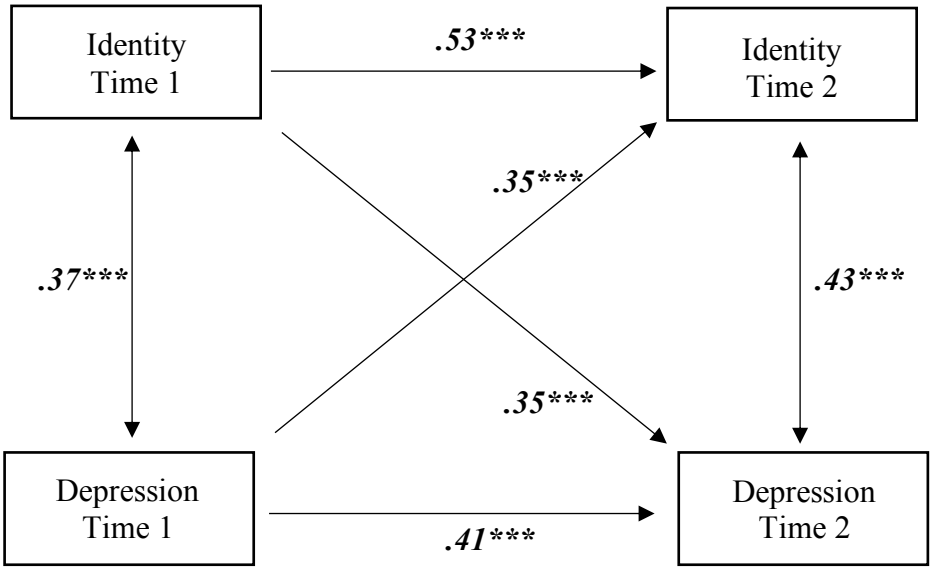
Linear Regression Analyses Explaining the Cross-Lagged Panel Model of Illness Beliefs About Personal Control of HS and Symptoms of Depression

Linear regression pathways	**β**	***SE***	***P* (95% *CI*)**
Personal control T1 -> Personal control T2	.23	.09	.019 (0.02, 0.43)
PHQ-2 T1 -> PHQ-2 T2	.41	.09	.001 (0.27, 0.61)
Personal control T1 -> PHQ-2 T1	-.12	.06	.228 (-0.18, 0.03)
PHQ-2 T1 -> Personal control T1	-.12	.16	.210 (-0.48, 0.09)
Personal control T2 -> PHQ-2 T2	-.31	.06	.001 (-0.32, -0.10)
PHQ-2 T2 -> Personal control T2	-.31	.13	.001 (-0.72, -0.22)
Personal control T1 -> PHQ-2 T2	-.14	.06	.104 (-0.20, .0.02)
PHQ-2 T1 -> Personal control T2	-.20	.14	.024 (-0.58, 0.06)

Note. β = standardised coefficient. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Figure 4.

Standardised Regression Coefficients (β) in a Cross-Lagged Panel Model Demonstrating the Effect of Illness Beliefs About Identity on Symptoms of Depression, and the Effect of Depressive Symptoms on Beliefs About Identity Over Time



Note. P values are bootstrapped (1000 samples).

*Coefficient is significant at $p < .05$, **coefficient is significant at $p < .01$, ***coefficient is significant at $p \leq .001$.

Table 15.

Linear Regression Analyses Explaining the Cross-Lagged Panel Model of Illness Beliefs About Identity and Symptoms of Depression

Linear regression pathways	**β**	***SE***	***P* (95% *CI*)**
Identity T1 -> Identity T2	.53	.08	.001 (0.35, 0.71)
PHQ-2 T1 -> PHQ-2 T2	.41	.09	.001 (0.27, 0.61)
Identity T1 -> PHQ-2 T1	.37	.07	.001 (0.16, 0.41)
PHQ-2 T1 -> Identity T1	.37	.09	.001 (0.30, 0.68)
Identity T2 -> PHQ-2 T2	.43	.06	.001 (0.23, 0.46)
PHQ-2 T2 -> Identity T2	.43	.10	.001 (0.34, 0.74)
Identity T1 -> PHQ-2 T2	.35	.06	.001 (0.16, .0.42)
PHQ-2 T1 -> Identity T2	.35	.11	.001 (0.24, 0.69)

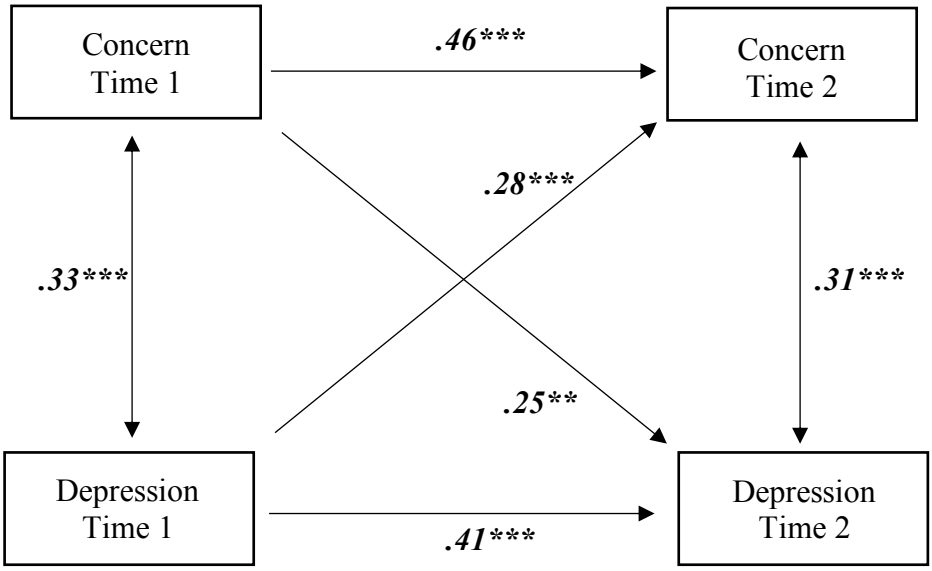
Note. β = standardised coefficient. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

The standardised regression coefficients for the paths between levels of concern about HS and depressive symptoms over time were all positive and statistically significant and are shown in Figure 5 (see Table 16 for further details). Synchronously the effect sizes were similar in both directions between depression symptoms and concern beliefs (.33 and .31). Both cross-lagged paths were significant and similar in effect size. Higher levels of depressive symptoms at baseline were associated with a higher level of concern at follow-up ($\beta = .28$, $p \leq .001$, 95% *CI* [0.20, 0.75]), and higher baseline concern about HS was associated with more depression symptoms at follow-up ($\beta = .25$, $p < .01$, 95% *CI* [0.09, 0.33]). This indicates that overall depression symptoms and concern beliefs had similar levels of influence on each other over time, and these associations were slightly lower than the influence on each other at baseline.

Figure 6 demonstrates the standardised regression coefficients for each pathway between emotional response to HS and symptoms of depression over time (see Table 17 for further details). All paths were statistically significant at $p \leq .001$. Trends of depressive symptoms and emotional response to HS were relatively stable across time (.41 and .60 respectively). Synchronously the directions of influence had similar effect sizes at each time point (.37 and .50). Both significant cross-lagged paths indicate that greater emotional response to HS predicted higher scores of depression symptoms over time ($\beta = .40$, $p \leq .001$, 95% *CI* [0.17, 0.35]) and higher levels of depressive symptoms predict greater emotional response to HS over time ($\beta = .35$, $p \leq .001$, 95% *CI* [0.24, 0.76]). Greater emotional response to HS at baseline had a stronger association with more depressive symptoms over time than baseline, indicating that emotional response at baseline may predict higher scores of depression symptoms at a later time point than at baseline assessment. Overall, depression symptoms and emotional response had a similar amount of influence on each other over time.

Figure 5.

Standardised Regression Coefficients (β) in a Cross-Lagged Panel Model Demonstrating the Effect of Concern About HS on Symptoms of Depression, and the Effect of Depressive Symptoms on Concern About HS Over Time



Note. P values are bootstrapped (1000 samples).

*Coefficient is significant at $p < .05$, **coefficient is significant at $p < .01$, ***coefficient is significant at $p \leq .001$.

Table 16.

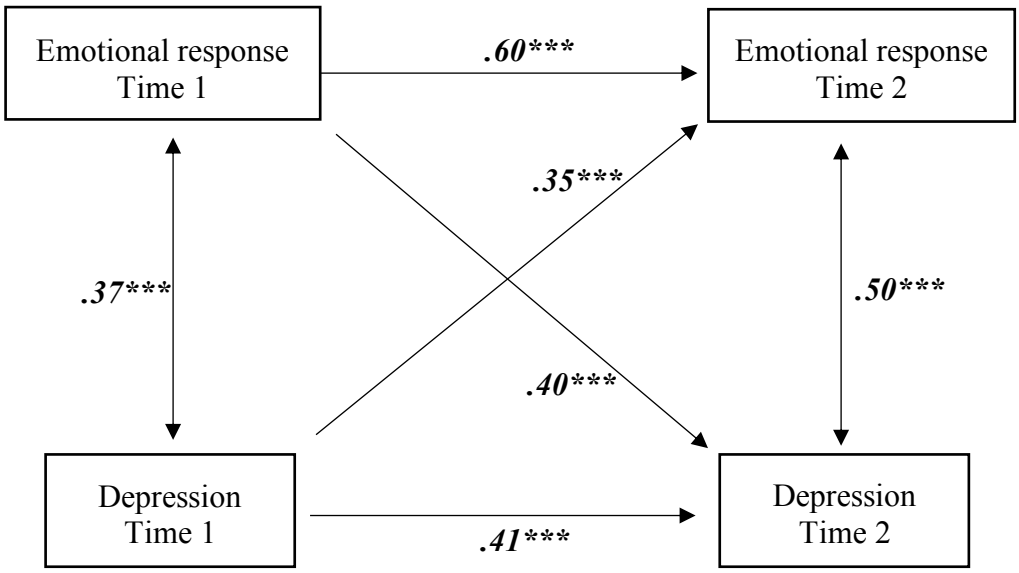
Linear Regression Analyses Explaining the Cross-Lagged Panel Model of Illness Beliefs About Concern About HS and Symptoms of Depression

Linear regression pathways	**β**	***SE***	***P* (95% *CI*)**
Concern T1 -> Concern T2	.46	.11	.001 (0.36, 0.84)
PHQ-2 T1 -> PHQ-2 T2	.41	.09	.001 (0.27, 0.61)
Concern T1 -> PHQ-2 T1	.33	.06	.001 (0.15, 0.38)
PHQ-2 T1 -> Concern T1	.33	.10	.001 (0.21, 0.59)
Concern T2 -> PHQ-2 T2	.31	.05	.001 (0.11, 0.31)
PHQ-2 T2 -> Concern T2	.31	.11	.001 (0.24, 0.69
Concern T1 -> PHQ-2 T2	.25	.06	.003 (0.09, .0.33)
PHQ-2 T1 -> Concern T2	.28	.14	.001 (0.20, 0.75)

Note. β = standardised coefficient. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

Figure 6.

Standardised Regression Coefficients (β) in a Cross-Lagged Panel Model Demonstrating the Effect of Emotional Response to HS on Symptoms of Depression, and the Effect of Depressive Symptoms on Emotional Response to HS Over Time



Note. P values are bootstrapped (1000 samples).

*Coefficient is significant at $p < .05$, **coefficient is significant at $p < .01$, ***coefficient is significant at $p \leq .001$.

Table 17.

Linear Regression Analyses Explaining the Cross-Lagged Panel Model of Emotional Responses to HS and Symptoms of Depression

Linear regression pathways	**β**	***SE***	***P* (95% *CI*)**
Emotional response T1 -> Emotional response T2	.60	.09	.001 (0.36, 0.73)
PHQ-2 T1 -> PHQ-2 T2	.41	.09	.001 (0.27, 0.61)
Emotional response T1 -> PHQ-2 T1	.37	.06	.001 (0.09, 0.34)
PHQ-2 T1 -> Emotional response T1	.37	.15	.001 (0.31, 0.91)
Emotional response T2 -> PHQ-2 T2	.50	.06	.001 (0.25, 0.46)
PHQ-2 T2 -> Emotional response T2	.50	.10	.001 (0.51, 0.88)
Emotional response T1 -> PHQ-2 T2	.40	.04	.001 (0.17, .0.35)
PHQ-2 T1 -> Emotional response T2	.35	.13	.001 (0.24, 0.76)

Note. β = standardised coefficient. *SEs, P* values, and 95% *CIs* are bootstrapped (1000 samples).

4. Discussion

Previous research into HS has mostly maintained a focus on the role of clinical characteristics in influencing health outcomes. The present study builds on research by Pavon Blanco et al. (2018) by gathering data from the participants at a follow-up appointment after baseline, allowing a longitudinal design. The first aim of this study was to examine whether illness perceptions at baseline predict quality of life and symptoms of anxiety and depression at follow-up, independently of HS severity. The second aim was to investigate the stability of these illness perceptions over time, and whether changes in illness perceptions were associated with the same health outcomes. The third aim was to explore the extent to which illness perceptions predict symptoms of depression, and the extent to which depressive symptoms predict illness perceptions over time.

Overall, illness perceptions at baseline explained a significant amount of variance in health outcomes at follow-up independent of disease severity when baseline health outcomes were not included in the model. In keeping with Pavon Blanco et al., (2018) HS severity at baseline explained very little of the variance in health outcomes at follow-up, both with and without baseline health outcomes being accounted for. Illness perceptions did not change significantly over time, apart from beliefs about experiencing high levels of symptoms (identity) and concern about HS. Changes in perceptions about how long HS will continue (timeline) were significantly associated with depressive symptoms and quality of life, levels of concern about HS were associated with anxiety symptoms and quality of life outcomes, and changes in beliefs about the consequences of HS were related to quality of life. Symptoms of depression and illness perceptions (consequences, identity, level of concern and emotional response to HS) were found to have an asymmetrical but reciprocal influence on each other over time, apart from personal control beliefs. Depression symptoms were found to predict personal control over time, but personal control beliefs were not predictive of depression scores over time.

4.1 Illness Perceptions and Health Outcomes

The number of illness perceptions scoring above mid-point at follow-up remained relatively similar to baseline. In line with Pavon Blanco et al.'s (2018) study, illness beliefs at follow-up showed that this cohort of people with HS continued to report higher

perceptions of consequences, experiences of symptoms, concern and emotional response than people with asthma, diabetes and myocardial infarction and lower personal and treatment control (Broadbent et al., 2006; Petrie et al., 2012). The most negatively scored illness perceptions were for timeline and concern about HS, and the most positive were for understanding of HS and how helpful treatment is. Previous research has indicated that higher control beliefs are often linked with shorter timeline beliefs (Petrie & Weinman, 2006), however the present cohort were recruited from tertiary care where participants are more likely to have experienced HS for longer and therefore views of a chronic timeline are more likely and often more in keeping with HS duration (Dufour et al., 2014). This length of time and experience with HS may also explain why their perceptions of understanding of HS is high.

Symptoms of anxiety and depression were also similar at baseline and follow-up with a slight reduction in the number meeting clinical threshold over time. Prevalence of clinically relevant anxiety scores in this cohort was higher than that found in previous studies of HS (Huilaja et al., 2018; Machado et al., 2019). Prevalence of clinically significant depression scores were slightly lower than that found in studies by Kluger, Ranta and Serlachius (2017) and Kurek et al. (2013) and higher than in the recent systematic review by Machado et al. (2019). Quality of life scores were slightly more variable between baseline and follow-up, however on average HS was having a very large impact on participants' lives. This extent of impact is consistent with previous research using the DLQI, and mean scores were actually higher than in several HS cohorts (Balieva et al., 2018; Calao et al., 2018; Kluger et al., 2017; Matusiak et al., 2010). Studies of other chronic conditions that have measured illness perceptions found lower scores of negative illness beliefs which may explain the higher prevalence rates of impaired quality of life and symptoms of anxiety and depression in HS (Broadbent et al., 2006; Petrie et al., 2012). This would correspond to past findings about decreases in psychological well-being and social outcomes (Gray & Rutter, 2007; Hagger & Orbell, 2003; Hagger et al., 2017; Morgan et al., 2014; Scharloo et al., 1998, 2000).

4.2 Predictive Ability of HS Severity and Illness Perceptions on Outcomes

Overall, illness perceptions contributed small improvements to all models and made significantly large improvements to models without baseline health outcomes included, whereas disease severity did not greatly improve any models. This is consistent

with the hypothesis that illness perceptions at baseline were a stronger predictor of quality of life and symptoms of anxiety and depression than HS severity (Hurley stage). The importance of illness perceptions in predicting health outcomes provides evidence for the dimensions included in the CSM (Leventhal et al., 1980; Leventhal et al., 1984), and shows that they are not directly linked to disease severity in HS. By distinguishing the influence of disease severity and illness perceptions these results highlight the need to acknowledge patient reported evaluations of HS in addition to clinical assessment in order to optimise health outcomes.

Anxiety

After controlling for demographics (age and gender), pain severity and anxiety symptoms at baseline both disease severity and illness perceptions did not significantly predict anxiety symptoms at follow-up. Unsurprisingly, this finding suggests that baseline anxiety symptoms are a strong predictor of anxiety symptoms at follow-up, however illness perceptions still explained more variance in anxiety over time than disease severity, in support of the hypothesis. Furthermore, when baseline anxiety scores were removed from the model illness perceptions were a significant predictor independently of Hurley stage, and made the largest contribution to anxiety scores at follow-up over and above demographics, pain and disease severity. This is in line with findings by Pavon Blanco et al. (2018) and other research (Broadbent et al., 2004, 2006; Jopson & Moss-Morris, 2003; Morgan et al., 2014; Petrie et al., 1996; Scharloo et al., 2000; Whittaker et al., 2007), and is in contrast to findings by Wahl et al. (2014). This indicates the importance of targeting illness perceptions in reducing risk of clinically significant anxiety, even if people with HS are not currently meeting threshold for anxiety disorders or are at lower levels of disease severity and pain.

Emotional response was a significant contributor in both models, which supports Pavon Blanco et al. (2018) and other cross-sectional findings in chronic conditions (Hagger et al., 2017; Morgan et al., 2014). The impact of emotional response increased greatly when baseline anxiety scores were removed, which is not surprising as the GAD-2 measures similar constructs to emotional response.

Depression

When baseline depression scores were accounted for in addition to demographics and pain, disease severity and illness perceptions were not significant predictors of depression symptoms over time. However, illness perceptions explained more variance than Hurley stage, and baseline depression scores became a non-significant contributor when illness perceptions were inserted into to the model. Baseline anxiety symptoms remained a significant predictor with disease severity and illness perceptions included in the model unlike baseline depression symptoms which indicates that baseline depression symptoms were a weaker predictor of follow-up depression scores than baseline anxiety symptoms were of follow-up anxiety scores. In contrast to Pavon Blanco et al.'s (2018) findings, when baseline depression scores were not included in the model, disease severity did not significantly predict depression symptoms independently of illness perceptions, whereas illness perceptions were a significant predictor. This finding supports the hypothesis, previous cross-sectional research (Broadbent et al., 2004, 2006; Jopson & Moss-Morris, 2003; Morgan et al., 2014; Pavon Blanco et al., 2018; Petrie et al., 1996; Scharloo et al., 2000; Whittaker et al., 2007) and longitudinal research in other chronic conditions (Llewellyn et al., 2007; Stafford et al., 2009). This is also evidence against findings by Wahl et al. (2014), suggesting that in people with HS illness perceptions may predict risk of depression at a later time point, independently of disease severity.

Emotional response was the most consistently significant variable contributing to anxiety and depression symptoms, both with and without baseline anxiety and depression scores included as predictors. This suggests that higher emotional response at baseline predicts more anxiety and depression symptoms at follow-up, which supports previous research into anxiety, distress and well-being (Hagger et al., 2017; Morgan et al., 2014). This corresponds to findings by Broadbent et al. (2015) and demonstrates the robustness of emotional response as a dimension in the BIPQ and emotional representations in the CSM (Leventhal et al., 1980). It should be noted, however, that the construct of emotional response may have a lot of overlap with measures of mood and anxiety and therefore its impact on these outcomes is not surprising.

Quality of Life

Scores on the baseline measure of quality of life were highly predictive of quality of life scores at follow-up, remaining consistently significant when demographics, pain, disease severity and illness perceptions were also measured. When baseline quality of life was removed, illness perceptions were a significant predictor of quality of life whereas disease severity was not. This result supports Pavon Blanco et al.'s (2018) findings and those from research into other conditions (Jopson & Moss-Morris, 2003; Morgan et al., 2014; Scharloo et al., 1998, 2000). The result also provides evidence against Wahl et al. (2014), and may indicate that Matusiak et al.'s (2010) finding that disease severity was the most important factor influencing quality of life and depression was because they had not included a measurement of illness perceptions.

Interestingly, when baseline quality of life had been removed, identity was a significant contributor. Consistent with findings in chronic fatigue syndrome (Gray & Rutter, 2007) this suggests that higher identity predicts poorer quality of life. Higher identity was also found to be associated with greater distress and poorer well-being and social functioning in other conditions (Hagger & Orbell, 2003; Hagger et al., 2017; Kemp et al., 1999; Scharloo, 1998). Identity can be indicative of the individual's view of the label and symptoms associated with this, and can be different to the view of clinicians treating the illness (Petrie & Weinman, 2006). This highlights the importance of assessing identity beliefs in people with HS regardless of their clinically defined HS severity, as symptoms or side effects may be misattributed symptoms to HS that may not be medically related (Petrie & Weinman, 2006).

In contrast to Pavon Blanco et al.'s (2018) and Gray and Rutter (2007), emotional response was not a significant contributor to prediction of quality of life outcomes. This may be due to the overarching variance explained by pain severity, which was a strong and significant contributor to quality of life over time when baseline quality of life had been removed. Pain had also contributed significantly to anxiety and depression scores when demographics and disease severity had been accounted for, however illness perceptions explained more variance and pain became non-significant. Taken together with other HS research into pain (Keary et al., 2019; Wolkenstein et al., 2007), the importance of assessing pain when considering the impact of HS on quality of life is evident.

Associations Between Illness Perceptions and Outcomes

Beliefs about timeline, personal control, and understanding were not significant predictors, and in contrast to findings by Pavon Blanco et al. (2018) and other studies of chronic illnesses (Hagger & Orbell, 2003; Hagger et al., 2017) perceptions about treatment control, negative consequences and concern were also not significant predictors. This contrast with other studies may be explained by the addition of pain severity as a predictor to the model, which has previously been indicated to influence feelings of anger and isolation in HS due to the lack of understanding about pain from others (Keary et al., 2019).

Overall, although most illness perceptions were not significant contributors independently, together they explained a significant amount of variance, and specifically higher identity and emotional response may be indicative of poorer outcomes over time. Therefore, interventions targeting emotional representations of HS and the reduction of attribution of symptoms to HS may improve health outcomes over time. Past interventions aimed at supporting people to tolerate emotional experiences have included mindfulness and acceptance-based techniques (Hayes, Strosahl & Wilson, 1999; Veehof, Trompetter, Bohlmeijer & Schreurs, 2016) and stress management interventions such as controlled breathing and progressive muscle relaxation (Varvogli & Darviri, 2011). An intervention study of people with breast cancer found that weekly group sessions of discussions about emotional experiences, writing about fears, cognitive exercises linked with core values, and techniques such as relaxation and imagery improved emotional well-being and coping efficacy (Cameron, Booth, Schlatter, Ziginskas & Harman, 2007).

4.3 Stability of Illness Perceptions Over Time

The majority of illness perceptions did not change significantly between baseline and follow-up. This suggests that in HS populations the majority of illness perceptions remain stable over time, as also found in studies of irritable bowel syndrome and lower back pain (Foster et al., 2008; Rutter & Rutter, 2007). The only illness beliefs that significantly changed were regarding the illness label and associated symptoms (identity) and the concern they have about having HS which both decreased over time. It is likely that for this cohort of participants their perception of the health threat had shifted from acute to chronic prior to this study due to recruitment being from a tertiary service. In line with the process of illness perception development proposed by the CSM (Leventhal et

al., 1980, 1984), these participants are likely to have experienced HS for longer than those in primary and secondary services and therefore may view HS as less treatable in a short duration of time and hold less concern about its progression. In line with the dynamic process in the CSM (Leventhal et al., 1980), decreases in identity and concern beliefs may be due to changes in coping responses as the participants gained more experience and information about symptoms and treatment over time (Leventhal, Phillips & Burns, 2016). These coping responses may have been evaluated and subsequently their beliefs about symptoms caused by HS were re-shaped (Leventhal et al., 1980, 2003).

The findings do not support previous research in diabetes and cardiac conditions that found understanding and timeline beliefs significantly increase, and emotional response decreases over time (Fischer et al., 2010; Lawson et al., 2008; Petrie & Weinman, 1997). Although not significant, the mean score for emotional response did decrease slightly over time, and the mean score for understanding increased slightly over time. This small increase in understanding could be explained by the acquisition of knowledge and experience with HS over time, however being in tertiary services it is likely that many participants may have plateaued in this area.

Association Between Changes in Illness Perceptions Over Time and Outcomes

Although changes in identity perceptions were significant over time, this change was not significantly related to outcomes at follow-up, whereas decreases in concern over time were significantly related to lower anxiety scores at follow-up. In terms of depression symptoms, participants whose beliefs about chronicity of HS increased over time had higher depression scores at follow-up, whereas increases in beliefs about personal control over HS over time was associated with lower depression scores. Surprisingly, increases in understanding over time were related to higher depression scores. This may be partly explained by the way that information about HS is shared and interpreted; people with HS may be basing their understanding on unreliable sources. This may increase depressive symptoms through ruminative processes and activation of depressive cognitions such as helplessness and hopelessness. Decreases in negative illness perceptions about consequences, timeline and concern about HS over time were related to better quality of life at follow-up. Reductions in emotional response and increases in beliefs about personal control were also close to significance. These findings provide further support for interventions aimed at reducing negative illness perceptions

(Broadbent et al., 2009; Petrie et al., 2002, 2012) and identifies specific illness beliefs to focus on. Targeting beliefs about consequences, timeline, concern, emotional response and controllability may reduce the risk of anxiety, depression and impaired quality of life.

4.4 Cross-Lagged Effects of Illness Perceptions and Symptoms of Depression

The findings from the cross-lagged analyses indicated mutual influences between depression symptoms and illness perceptions (apart from personal control) regardless of time, suggesting no temporal precedence. Personal control beliefs were not significantly predictive of depression scores at baseline or follow-up, whereas depression scores were predictive of personal control beliefs over time but not at baseline.

The predictive ability of depression symptoms on personal control over time is not in line with findings by Chilcot et al. (2013) who found no association between the trajectory of depression and personal control in people with renal problems, but may fit with the argument that other variables such as proinflammatory cytokines involved in HS may precede development of depression in HS (Goldstein, Kemp, Soczynska & McIntyre, 2009; Kelly & Prens, 2016; Kohler et al., 2017; van der Zee et al., 2011). These symptoms of depression may influence how people perceive the amount of control they have over HS. This finding of depression symptoms leading to lower personal control beliefs also supports literature by Bower (1981), Teasdale (1983) and Tversky and Kahneman (1974). Participants' baseline depression symptoms may have increased access to negative cognitions and memories, and feelings of hopelessness and low energy and motivation are likely to have impacted coping behaviours. Rumination is a common process in low mood that has been found to impair concentration, central executive functioning and problem-solving (Lyubomirsky, Kasri & Zehm, 2003; Noelen-Hoeksema, 2000; Watkins and Brown, 2002). Difficulties with problem-solving and increases in cognitive biases such as catastrophising, predictive thinking and minimising about their ability to have control over HS may have impacted their coping appraisals, in particular beliefs about personal control over HS and level of concern about the future. This is consistent with the theory of learned helplessness (Maier & Seligman, 1976). Participants may also have believed that others have been able to change their outcomes and impact of HS, whereas they were not able to (Abramson, Seligman & Teasdale, 1978). In addition, increased attention towards negative elements and physical symptoms of their current experience of HS are likely to impact their interpretation of how HS is

impacting their life. This demonstrates how symptoms of depression can inform the development of illness perception in the feedback loop described by Leventhal et al. (1980) and Petrie and Weinman (2006). This also demonstrates the vicious cycle of behaviours, emotions and negative cognitions reinforcing each other as described by Beck (1967), that may also explain the overall mutual influence of illness perceptions and symptoms of depression on each other both at the same time points and over time.

The association between higher depressive symptoms and lower personal control over time is also consistent with the theory of learned helplessness (Abramson et al., 1978; Maier & Seligman, 1976). Participants who are depressed may hold more negative beliefs about believe that others have been able to change their outcomes and impact of HS, whereas they are not able to and therefore have a sense of helplessness

The strongest reciprocal influence was between negative beliefs about consequences of HS and symptoms of depression which was expected based on cross-sectional findings by Pavon Blanco et al. (2018). Emotional response was the only illness perception that had a stronger influence on depressive symptoms over time rather than at baseline. This suggests that people who are scoring more highly on the emotional response item at a baseline assessment may be more likely to develop more symptoms of depression over time. This has implications for referring people to illness perception interventions who are scoring highly on the emotional response regardless of their depression score, and for interventions to specifically target emotional response and prevent depressive symptoms from worsening. As previously stated, this finding should be interpreted with caution due to the likely overlap of the construct with measures of depression.

Overall, Leventhal et al.'s (1980) CSM has been useful across research to understand the impact of illness representations as determinants on outcomes in different illnesses. The findings of this project also indicate that illness representations have a predictive impact on health outcomes in HS, however, the cross-lag relationships between outcomes (depression symptoms) and illness perceptions were not specified in the model. Although the model demonstrates parallel processing of cognitions and emotions, it is not clear how these strands interact. It will be important for future research to look at their

interactions rather than treating them as disconnected processing entities (Revenson & Diefenbach, 2019).

4.5 Strengths and Limitations

To date, this is the first longitudinal study investigating the predictive ability of illness perceptions on health outcomes over time in an HS population. This improves on previous HS research as it is better able to infer the direction of causality on outcomes than cross-sectional studies, and is therefore able to inform screening procedures in clinical practice regarding risk of anxiety, depression and impaired quality of life. It is also the first study to explore stability of illness perceptions over time in HS, and the impact this has on outcomes. These findings can directly inform psychological interventions to reduce negative outcomes, by referring to unique impact of each illness perception and their direction of change over time. The cross-lagged analysis in this study also addresses the gap in literature about the influence of depressive symptoms on illness perceptions. This is extending the literature on development of illness perceptions and how these can be modified at intervention level. The validated and reliable outcome measures allow for this study to be compared to previous studies and replicated in future research, and is directly applicable to measures used routinely in clinical practice. Furthermore, this study is the first to account for the impact of pain severity on outcomes in HS alongside illness perceptions and disease severity, as this has become increasingly evident as an influential factor in past HS research.

This study has several limitations. Although it is longitudinal in design, absolute causality cannot be established as the possibility of other explanations and variables influencing outcomes cannot be ruled out, and the study is not experimental or intervention based. In line with this, confounding factors such as HS treatment and/or psychological treatments at baseline were not controlled for in the analysis and may have influenced the outcomes. A substantial limitation of this study is sampling bias. Firstly, there were no participants over the age of 63, therefore findings may not be generalisable to older adults with HS. It should be noted however, that research has found HS prevalence may reduce over time (Alikhan, Lynch & Eisen., 2009) with significantly lower prevalence in those age 55 and older compared to younger ages (Revuz et al., 2008). Generalisability may also be more limited due to recruitment from one London teaching hospital in a tertiary service of patients with more severe HS. This was evident in the

statistics of HS severity, with 73-75% of the sample having severe HS compared to 15-20% having mild HS. Due to the majority of participants being at higher Hurley stages, the findings of this study may not be representative of participants with milder forms of HS. Furthermore, the sample size was smaller than required for a regression analysis with up to 15 predictors, according to Cohen (1988) and Green (1991). Cohen (1998) stated that more than 150 participants are required to detect a medium effect size, and Green's (1991) rule indicates a sample of 170 ($50 + 8k$, k = number of predictors) would be required therefore findings from the regressions should be interpreted with caution.

A further limitation is that findings are based on disease severity measured by Hurley staging, which recent research has deemed inaccurate as it does not assess current levels of inflammation (Kimball et al., 2016; Scuderi et al., 2017). It is also unable to measure decreases from stage 2 due to the irreversibility of scarring which is the main feature of Hurley staging (van der Zee & Jemec, 2015). Findings may therefore not reflect the true predictive ability of disease severity on outcomes, and may not be directly applicable to future research and clinical practice as more dynamic measures continue to be implemented (Kimball et al., 2014). Other measurement limitations include the use of a single visual analogue scale to measure pain severity and the single item measures for each illness perception component on the BIPQ. These unidimensional methods risk oversimplifying the complexity of pain and each illness perception and thus results may have limited validity (Chapman & Syrjala, 1990; Revenson & Diefenbach, 2019).

The results of the cross-lagged panel analyses should also be interpreted with caution due to violation of several assumptions that this is based on (Kearney, 2017). Synchronicity was not fully adhered to due to participant data being collected at different clinic dates, with times between baseline and follow-up ranging from approximately 6 to 20 months. This range of time between measurements will have also limited the initial analyses of stability of illness perceptions over time. It is also possible that assumptions of stability and stationarity may have been violated due to potential for inter-individual differences and other variables (e.g. trait influences and different levels of pain) that may have impacted changes in causal structure (Kearney, 2017). We can also not assume that variables were measured without error. Therefore, findings may be biased and should be interpreted in terms of influence rather than direct causality. The time lag is assumed to be conceptually viable based on past longitudinal findings of illness perceptions

predicting depression (Llewelyn et al., 2007), however it is not clear whether this time frame is too short to identify effects of mood on illness perceptions. There were also some differences in the synchronous effect sizes between baseline and follow-up, therefore other factors may have impacted the findings, such as how long participants had been living with HS and treatment effects. Overall, the use of regression to measure panel data is reported to be a plausible method, however further research is required into robust statistical techniques for assessing causal influence (Rogosa, 2017).

4.6 Future Research

Following on from the limitations, if this study is to be replicated in future research a larger sample should be recruited with a minimum of 170 participants to sufficiently power the study. It would be beneficial to include the causes component of the BIPQ in future research as this will provide further insight into outcomes over time and has already been shown to be an effective illness perception to target in psychological interventions (Broadbent et al., 2015). In addition to this, variables of current HS treatment and any ongoing psychological interventions would also be useful to include to control for treatment effects. To build on the findings of this study and the CSM theoretical model, future research could also examine coping mechanisms in an HS population and the impact this has on outcomes, and the extent to which psychological variables and disease severity predict illness perceptions. The findings regarding pain as a predictor of outcomes supports perspectives of patients, carers and clinicians in a study by Ingram et al. (2014) that pain management is a priority for HS research; investigating whether pain is a mediator of the impact of illness perceptions on outcomes would be useful particularly in clinical practice. This study is the first to explore the bi-directional links between illness perceptions and depression in an HS cohort over two time points. Studies of coronary heart disease and kidney failure have started to explore the association between illness perceptions and trajectories of psychological distress including depression and anxiety (Chilcot et al., 2013, 2019), therefore future research should aim to explore patterns between illness perceptions and emotions using trajectory analysis over multiple time points. It would also be beneficial to extend research into the cross-lagged influences of illness perceptions on outcomes by looking at other factors that may influence the link between illness perceptions and mood.

HiSCR is a more recently developed and validated HS severity tool which allows for simple assessment of disease severity over time. It has been used in clinical trials of treatments for HS (Kimball et al., 2016), and recommended by the National Institute for Health and Care Excellence (NICE, 2016). In comparison to Hurley stage and other HS scoring systems, HiSCR increases sensitivity to HS-specific lesions and is more responsive to the acute phase and improvements in disease activity (Kimball et al., 2016). Therefore, future research would benefit from replicating this study but using HiSCR as the measure of disease severity in order to assess whether this more accurate measure has stronger predictive ability on outcomes than Hurley staging and illness perceptions.

4.7 Clinical Implications

The finding that illness perceptions were a stronger predictor of quality of life and symptoms of anxiety and depression in people with HS over and above disease severity implies that clinicians should assess illness perceptions as well as clinical characteristics of HS in order to identify people at risk of poorer outcomes over time. In particular, people reporting higher emotional response to HS may indicate risk of anxiety and depression over time, and higher identity beliefs and pain severity may indicate risk of quality of life impairment over time. It may also be the case that people with HS could present with symptoms of depression without significantly negative illness beliefs (personal control in particular). The finding that depression symptoms were not predictive of personal control beliefs at baseline but were at follow-up has implications for screening and intervention. People with HS who report depressive symptoms at an assessment may be more likely to develop lower beliefs in their personal control over HS, regardless of their current beliefs about personal control. Referring them for support with symptoms of depression or brief psychoeducation may reduce this risk and the negative impact this may have on psychological well-being (Bradley, Lewis, Jennings & Ward, 1990; Hagger & Orbell, 2003; Hagger et al., 2017; Morgan et al., 2014; Shillitoe & Christie, 1990). This is particularly relevant to the clinics that the current participants attended as the illness perception measure was only administered every 6 months compared to depression, anxiety, and quality of life measures that are administered on every visit.

A further clinical implication is that psychological interventions to modify illness perceptions such as those demonstrated in other research (Broadbent et al., 2009; Petrie et al., 2002, 2012) may be imperative alongside dermatological treatment in

multidisciplinary care in order to optimise health outcomes over time. A systematic review by Jones, Smith and Llewellyn (2015) evaluated nine interventions using the CSM to change illness beliefs and adherence behaviour, and only found one that had a large significant effect on control and cure illness perceptions (Petrie et al., 2002). This intervention used information about antecedents, problem-solving, action planning (how to cope with distress and negative consequences) and reattribution, and may therefore be useful in future interventions aimed at modifying illness perceptions. The findings showing mutual influence between illness perceptions and depression further support implications for specialised interventions targeting illness perceptions, in addition to options to offer referrals into a depression pathway.

The changes in illness perceptions over time and the reciprocal influence between symptoms of depression and illness perceptions indicate that focusing solely on cognitions may not be the only intervention worth exploring. Cognitive behavioural interventions may be useful in breaking the cycle between depression and negative cognitions (Beck, 1967; Teasdale, 1983), and it has been recommended that CSM-based interventions should focus on both threat-focused and emotion-focused regulation strategies (Cameron et al., 2007; Cameron & Jago, 2008). In particular, psychological interventions could include strategies aimed at restructuring and challenging negative beliefs about consequences, timeline and controllability, behavioural interventions such as behavioural activation, and developing emotional regulation strategies. In light of Orbell and Phillips (2019) discussion regarding the influence of attentional and interpretational biases, they suggest that interventions address automatic processes as well as beliefs. This has been found to be effective in changing beliefs and medication adherence in patients following a stroke (O'Carroll, Chambers, Dennis, Sudlow, & Johnston, 2014). Interventions could include planning responses to illness or treatment experiences and rehearsing these; this may improve attitudes towards managing threats and their self-efficacy for managing them (Orbell & Phillips, 2019). Incorporating these different aspects into interventions may reduce the prevalence of anxiety, depression and impaired quality of life in people with HS.

4.8 Conclusions

This study was the first to investigate the impact of demographics, pain, disease severity and illness perceptions on longitudinal outcomes of anxiety and depression

symptoms and quality of life in HS. The results showed that illness perceptions were predictive of health outcomes independently of disease severity and accounted for more variance in all outcomes. It was also found that most illness perceptions remain stable over time (although reductions in negative illness beliefs were related to better outcomes over time), and the relationships between illness perceptions and symptoms of depression over time were bi-directional. The findings of this study emphasise the importance of patients' evaluations of their illness, as well as clinician rated severity; milder disease severity may not be indicative of lower risk of anxiety, depression and impaired quality of life. It is hoped that this study will encourage routine assessment of illness beliefs in people with HS, and emphasise the need for further research and development of interventions to modify illness perceptions in order to improve health outcomes. Further research is required into the development and predictive ability of illness perceptions in HS, and will benefit from recruiting a larger sample from different services and taking into consideration dermatological and psychological treatment that participants are undergoing at the time of study.

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Appendix A – Health Research Authority Approval Letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Professor John Weinman
Institute of Pharmaceutical Science
King's College London
5th Floor, Franklin-Wilkins Building, 150 Stamford Street
SE1 9NH

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

06 February 2019

Dear Professor Weinman

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**The role of disease severity and illness perceptions in predicting depression, anxiety and quality of life in patients with Hidradenitis Suppurativa: a longitudinal study**
IRAS project ID:	**254896**
Protocol number:	**1**
Sponsor	**King's College London**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

This is a single site study co-sponsored by the site. The sponsor R&D office will confirm to you when the study can start following issue of HRA and HCRW Approval.

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The attached document *"After HRA Approval – guidance for sponsors and investigators"* gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Professor Reza Razavi
Email: reza.razavi@kcl.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **254896**. Please quote this on all correspondence.

Yours sincerely

Thomas Fairman
HRA Assessor

Email: hra.approval@nhs.net

Copy to: *Professor Reza Razavi, King's College London, (Sponsor Contact)*
Miss Jennifer Boston, Guy's & St Thomas' Foundation NHS Trust, (Lead NHS R&D Contact)

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [254896 KCL Insurance Letter 26/11/18]	1	26 November 2018
IRAS Application Form [IRAS_Form_01022019]		01 February 2019
Letter from funder [254896 Research funding confirmation letter 261118]	1	26 November 2018
Other [254896 KCL Employer Liability Certificate 26/11/18]	1	26 November 2018
Research protocol or project proposal [254896 Protocol 11/01/19]	1	11 January 2019
Summary CV for Chief Investigator (CI) [254896 CV John Weinman 26/11/18]	1	26 November 2018
Summary CV for student [254896 CV Kelsey Jones 26/11/18]	1	26 November 2018
Summary CV for supervisor (student research) [254896 CV John Weinman 26/11/18]	1	26 November 2018
Summary CV for supervisor (student research) [254896 CV Mark Turner 26/11/18]	1	26 November 2018

IRAS project ID	254896

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	This is a non-commercial single site study taking place in the NHS where that single NHS organisation is also the study sponsor. Therefore no study agreements are expected.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study.
4.3	Financial arrangements assessed	Yes	Study funding has been secured from Kings College London.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any	Yes	No comments

Section	Assessment Criteria	Compliant with Standards	Comments
	applicable laws or regulations		
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Not Applicable	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
This is a non-commercial single site study taking place in the NHS where that single NHS organisation is also the study sponsor. Therefore there is only one site type involved in the research. If this study is subsequently extended to other NHS organisation(s) in England and Wales, an amendment should be submitted, with a Statement of Activities and Schedule of Events for the newly participating NHS organisation(s). The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS or on the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net, or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Principal Investigator should be appointed at study sites. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
As a non-commercial study undertaken by local staff, it is unlikely that letters of access or honorary research contracts will be applicable. Where arrangements are not already in place, researchers undertaking any of the research activities listed in A18 of the IRAS form would be expected to obtain a Letter of Access. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed).

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix B – Confirmation Email of GSTFT Participation

From: Liu Xin <Xin.Liu@gstt.nhs.uk>
Sent: 18 February 2019 16:49
To: Turner Mark <Mark.Turner@gstt.nhs.uk>
Cc: Jones, Kelsey <kelsey.jones@kcl.ac.uk>; Weinman, John <john.weinman@kcl.ac.uk>; Flohr, Carsten <carsten.flohr@kcl.ac.uk>; Jones Jacky <Jacky.Jones@gstt.nhs.uk>
Subject: [Disease severity and illness perceptions in Hidradenitis Suppurativa] IRAS: 254896Confirmation of GSTFT participation

Dear Dr Tuner,

Study Title: Disease severity and illness perceptions in Hidradenitis Suppurativa
Sponsor: KCL co-sponsor GSTT
Chief Investigator: Prof John Weinman

Guy's and St Thomas' NHS FT has agreed to host your research study. Your study can therefore now start at GSTFT.

You have committed to recruit 232 participants between 18/02/2019 and 30/05/2020. The Trust is performance managed nationally by the NIHR. You will be expected to recruit your first participant by this date 20/03/2019 to meet your performance target.

Please note your responsibilities in the attached 'Conditions of GSTFT participation'. These conditions must be adhered to for the Trust to continue to host and support your research.

Documents approved:

Document	*Version*	*Date*
254896_Protocol_version1_110119	1.0	11/01/2019

If you wish to make any changes to the approved documents, please contact the R&D department or refer to our guidance on submitting amendments.

We are piloting a small survey for general feedback on the performance of the non-commercial R&D department. We would appreciate it if you could take a few minutes to let us know what you think:https://goo.gl/forms/46Q2bF4a2vCuwufP2

Best wishes,
Xin

Xin Liu, R&D Governance Facilitator (Non-commercial team)
NIHR GSTFT/KCL Biomedical Research Centre
16th floor, Tower Wing, Guy's Hospital
Great Maze Pond,
London
SE1 9RT
Tel: 020 7188 7188 ext: 51199 F: 0207 188 3472
E: xin.liu@gstt.nhs.uk | W: www.guysandstthomas.nhs.uk/

Appendix C – Confirmation Email That King's College Ethics Not Required

From: Patterson, James [mailto:james.2.patterson@kcl.ac.uk]
Sent: 02 August 2019 15:58
To: Heard Clare <Clare.Heard@gstt.nhs.uk>
Subject: RE: 254896_Registration with KCL ethics?

Dear Clare,

Thank you for your e-mail.

It seems to me that the researcher is using data that has been collected entirely from NHS patients. That being the case, the study does not require ethical approval from the College.

I hope this is helpful. Please let me know if you have any other questions.

Best wishes,

James

James Patterson
Senior Research Ethics Officer
Research Ethics Office
King's College London
4/16 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
LONDON SE1 9NH

Telephone: 020-7848-4077

E-mail: james.2.patterson@kcl.ac.uk

Appendix D – Health Research Authority Amendment Confirmation Email

From: hra.approval@nhs.net <noreply@harp.org.uk>
Sent: 30 September 2019 09:25
To: Weinman, John <john.weinman@kcl.ac.uk>; Razavi, Reza <reza.razavi@kcl.ac.uk>; Jones, Kelsey <kelsey.jones@kcl.ac.uk>
Subject: IRAS 254896. Amendment categorisation and implementation information

Amendment Categorisation and Implementation Information

Dear Professor Weinman,

IRAS Project ID:	254896
Short Study Title:	Disease severity and illness perceptions in Hidradenitis Suppurativa
Date complete amendment submission received:	16.9.19
Amendment No./ Sponsor Ref:	1
Amendment Date:	17.8.19
Amendment Type:	Non-substantial
Outcome of HRA and HCRW Assessment	**This email also constitutes HRA and HCRW Approval for the amendment,** and you should not expect anything further.
Implementation date in NHS organisations in England and Wales	35 days from date amendment information together with this email, is supplied to participating organisations **(providing conditions are met)**
Implementation date in NHS/HSC organisations in Northern Ireland and/or Scotland	4.11.19 **(providing conditions are met)**
For NHS/HSC R&D Office information	
Amendment Category	**A**

Thank you for submitting an amendment to your project. We have now categorised your amendment and please find this, as well as other relevant information, in the table above.

What should I do next?

Please read the information in IRAS, which provides you with information on how and when you can implement your amendment at NHS/HSC sites in each nation, and what actions you should take now.

If you have participating NHS/HSC organisations in any other UK nations please note that **we will** forward the amendment submission to the relevant national coordinating function(s).

If not already provided, please email to us any regulatory approvals (where applicable) once available.

When can I implement this amendment?

You may implement this amendment in line with the information in IRAS. Please note that you may only implement changes described in the amendment notice.

Who should I contact if I have further questions about this amendment?

If you have any questions about this amendment please contact the relevant national coordinating centre for advice:

- England – hra.amendments@nhs.net
- Northern Ireland – research.gateway@hscni.net
- Scotland – nhsg.NRSPCC@nhs.net
- Wales – HCRW.amendments@wales.nhs.uk

Additional information on the management of amendments can be found in the IRAS guidance.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/.

Please do not hesitate to contact me if you require further information.

Kind regards

Laura Chappell

Health Research Authority

Ground Floor | Skipton House | 80 London Road | London | SE1 6LH

E.hra.amendments@nhs.net

W. www.hra.nhs.uk

Appendix E – GSTT R&D Approval Email of Non-Substantial Amendment

From: Adeyemi Lola <Lola.Adeyemi@gstt.nhs.uk>
Sent: 02 October 2019 09:31
To: Turner Mark <Mark.Turner@gstt.nhs.uk>
Cc: Weinman, John <john.weinman@kcl.ac.uk>; Jones, Kelsey <kelsey.jones@kcl.ac.uk>
Subject: Confirmation of continued capacity and capability - Disease severity and illness perceptions in Hidradenitis Suppurativa

Dear Dr Turner

Study Title:	Disease severity and illness perceptions in Hidradenitis Suppurativa
Amendment Number:	Minor amendment 1
R&D Number:	254896
IRAS Number:	254896
CI:	Prof John Weinman
PI:	Dr Mark Turner
Sponsor:	King's College London/Guy's and St Thomas' NHS Foundation Trust
Health Research Authority (REC) Substantial or Non-substantial:	Non-Substantial

Guy's and St Thomas' NHS Foundation Trust has agreed to continue to host your research study. You can implement the above amendment here at the Trust with immediate effect.

Documents approved:

Document Title	Version	Date
254896_non-substantialminor-amendmentss_160819	-	17/08/2019
254896_Protocol_version2_160819 final	2.0	16/08/2019
254896_Protocol_version2_160819	2.0	16/08/2019
CV research ER	-	-
FF CV_July2019	-	09/07/2019
Fwd IRAS 254896 Amendment categorisation and implementation information	-	30/09/2019

Kind regards
Lola

Lola Adeyemi
Research Governance Coordinator
NIHR GSTFT/KCL Biomedical Research Centre
16th floor, Tower Wing, Guy's Hospital
Great Maze Pond
London SE1 9RT
Tel: 020 7188 7188 Ext: 51389
Email: lola.adeyemi@gstt.nhs.uk

Appendix F – IMPARTS Oversight Committee Approval Emails

From: Rayner, Lauren <lauren.rayner@kcl.ac.uk>
Sent: 17 April 2019 10:14
To: Jones, Kelsey <kelsey.jones@kcl.ac.uk>
Cc: Turner Mark <Mark.Turner@gstt.nhs.uk>; Weinman, John <john.weinman@kcl.ac.uk>; Abdelrahman Wedad <Wedad.Abdelrahman@gstt.nhs.uk>
Subject: IMPARTS Research Application - HS

Dear Kelsey

The Oversight Committee are happy with the revised application, which I can confirm has now been approved.

We will now prepare a list of HS patient Hospital numbers to send to Dr Abdelrahman.

Best wishes,

Lauren

IMPARTS Oversight Committee Amendment Approval Email

From: Rayner, Lauren <lauren.rayner@kcl.ac.uk>
Sent: 17 September 2019 13:53
To: Jones, Kelsey <kelsey.jones@kcl.ac.uk>
Subject: RE: IMPARTS Research Application - HS

Hi Kelsey

Thanks for the update.

This should be fine. You won't need to reapply to the Oversight Committee on the basis of these changes, but please do send me an updated version of your IMPARTS research application for our records.

Best wishes,

Lauren

Appendix G – PHQ-2 and GAD-2 Screening Questionnaire

phq-2 & gad-2 screening

PHQ-2 GAD-2	*Over the **last 2 weeks** (or other agreed time period) how often have you been bothered by any of the following problems?*	*not at all*	*several days*	*more than half the days*	*nearly every day*
1.	Little interest or pleasure in doing things	*0*	*1*	*2*	*3*
2.	Feeling down, depressed, or hopeless	*0*	*1*	*2*	*3*
3.	Feeling nervous, anxious or on edge	*0*	*1*	*2*	*3*
4.	Not being able to stop or control worrying	*0*	*1*	*2*	*3*

Questions 1 & 2 screen for depression, with a total score of 3 or more for these two items suggesting the strong possibility of clinical depression.

Questions 3 & 4 screen for anxiety (GAD, panic, PTSD & social anxiety), with a total score of 3 or more for these two items suggesting the strong possibility of clinical anxiety.

Kroenke, K., R. L. Spitzer, et al. (2003*). "The Patient Health Questionnaire-2: validity of a two-item depression screener."* Med Care 41(11): 1284-1292.

Kroenke, K., R. L. Spitzer, et al. (2007*). "Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection."* Ann Intern Med 146(5): 317-325.

Appendix H – DLQI Screening Questionnaire

DERMATOLOGY LIFE QUALITY INDEX (DLQI)

Hospital No: …… **Date:** ……

Name: …… **Score:** ……

Address: …… **Diagnosis:** ……

……

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick (✓) one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	Not relevant ❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒ ❒	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒

Please check you have answered EVERY question. Thank you.

DERMATOLOGY LIFE QUALITY INDEX (DLQI) - INSTRUCTIONS FOR USE

The Dermatology Life Quality Index questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self explanatory and can be simply handed to the patient who is asked to fill it in without the need for detailed explanation. It is usually completed in one or two minutes.

SCORING

The scoring of each question is as follows:

Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question 7, 'prevented work or studying'	scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

HOW TO INTERPRET MEANING OF DLQI SCORES

0 – 1	no effect at all on patient's life
2 – 5	small effect on patient's life
6 – 10	moderate effect on patient's life
11 – 20	very large effect on patient's life
21 – 30	extremely large effect on patient's life

REFERENCES

Finlay AY and Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; **19:**210-216.

Basra MK, Fenech R, Gatt RM, Salek MS and Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. *Br J Dermatol* 2008; **159:**997-1035.

Hongbo Y, Thomas CL, Harrison MA, Salek MS and Finlay AY. Translating the science of quality of life into practice: What do dermatology life quality index scores mean? *J Invest Dermatol* 2005; **125:**659-64.

There is more information about the DLQI, including over 85 translations, at www.dermatology.org.uk. The DLQI is copyright but may be used without seeking permission by clinicians for routine clinical purposes. For other purposes, please contact the copyright owners.

Appendix I – BIPQ Screening Questionnaire

The Brief Illness Perception Questionnaire

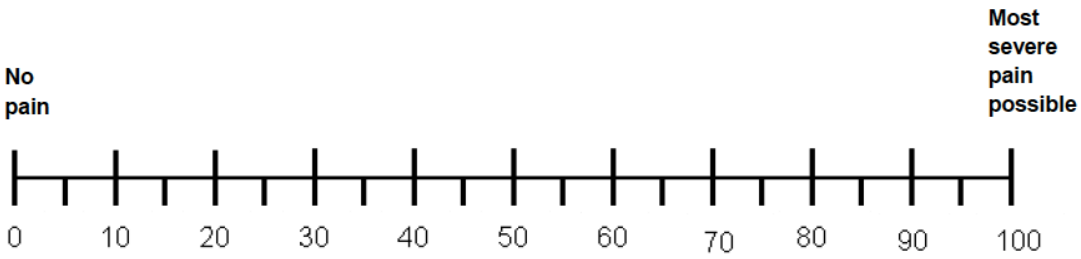
For the following questions, please circle the number that best corresponds to your views:

How much does your illness affect your life?										
0 no affect at all	1	2	3	4	5	6	7	8	9	10 severely affects my life
How long do you think your illness will continue?										
0 a very short time	1	2	3	4	5	6	7	8	9	10 forever
How much control do you feel you have over your illness?										
0 absolutely no control	1	2	3	4	5	6	7	8	9	10 extreme amount of control
How much do you think your treatment can help your illness?										
0 not at all	1	2	3	4	5	6	7	8	9	10 extremely helpful
How much do you experience symptoms from your illness?										
0 no symptoms at all	1	2	3	4	5	6	7	8	9	10 many severe symptoms
How concerned are you about your illness?										
0 not at all concerned	1	2	3	4	5	6	7	8	9	10 extremely concerned
How well do you feel you understand your illness?										
0 don't understand at all	1	2	3	4	5	6	7	8	9	10 understand very clearly
How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?										
0 not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 extremely affected emotionally
Please list in rank-order the three most important factors that you believe caused <u>your illness</u>. *The most important causes for me:-*										
1. _____										
2. _____										
3. _____										

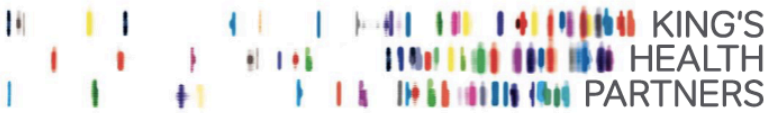
Appendix J – Pain Visual Analogue Scale (VAS)

Pain severity

Please click on the scale below to indicate the severity of your pain over the past month:



Appendix K – King's Health Partners Honorary Passport



An Academic Health Sciences Centre for London — Pioneering better health for all

Honorary Passport

For

Name	Kelsey Jones	
Substantive Employer	South London and Maudsley NHS Foundation Trust	
Date issued	10/12/2019	
Issued By (HR)	Linda Ekhator	
Valid From	10/12/2019	
End date	30/09/2020	
Signed by (HR)	Linda Ekhator	**Date:** 10/12/2019
Signed by Employee		**Date**

1. Scope of Honorary passport:

The terms of the honorary passport apply to work at any of the designated sites within Kings Health Partners, namely Guy's and St Thomas' NHS Foundation Trust, Kings College Hospital NHS Foundation Trust, South London and the Maudsley NHS Foundation Trust and Kings College London ("the Founders").

The terms of the honorary passport will apply to you if you are an employee of a Founder and have accepted a post that requires you to perform duties, whether permanently, regularly or occasionally, on the premises of any Founder other than your substantive employer.

In such case your substantive employer will confirm to you, together with the terms and conditions of your post, the fact that the honorary passport applies to you and in respect of which Founder or Founders it applies. You will be informed by your substantive employer that by accepting such post you will also be accepting the terms of the honorary passport.

2. Status of Honorary Passport Holder:

2.1 The honorary passport does not constitute a contract of employment with any of the Founders and you will not be entitled to any payment as a result of the terms of the honorary passport applying to you. This will not affect the terms and conditions of the contract of employment you already hold with your substantive employer.

2.2 The honorary passport will terminate immediately if you cease to be employed by the Founder, who is your substantive employer, for whatever reason (including dismissal with or without notice and your own voluntary resignation).

3. Terms of Honorary Passport:

3.1. Honorary passports are not time limited, with the exception of section 2.2 above. Where the passport is time limited, the period during which the honorary passport applies will be detailed within the passport itself. This confirmation will also set out to whom you are to report at the Founder in respect of whom the honorary passport applies (i.e. host manager).

3.2. During the period to which the honorary passport applies you must abide by all policies and procedures of the Founder on whose premises you perform duties. [These policies are available on the relevant Founder's intranet and on request from the relevant Founder's HR Department.]

3.3. Staff undertaking clinical duties should have regular reviews with their academic and clinical line managers through agreed joint appraisal mechanisms. For Clinical academic staff, there will be a formal job plan of fixed commitments which will be reviewed on an annual basis with their academic and clinical line managers through joint appraisal mechanisms.

In line with the arrangements for the new consultant contract for clinical academics, a job plan for clinical and academic activity will be agreed with the appointee. The post is full-time (a minimum of 10 programmed activities under the new consultants' contract, of which 5 will be clinical). The appointment will be made subject to the agreement of this plan which will follow the appropriate national and local guidance in ensuring suitable acknowledgement for activities required of the post holder by both clinical and academic Founders.

3.4. You must acknowledge your own limitations and decline any duties or responsibilities for which you do not have the necessary skills, experience or training.

3.5. You must take every reasonable care for the health and safety of yourself and of others. You must not intentionally or recklessly interfere with, or misuse, anything provided in the interests of health, safety or welfare.

3.6. During the period to which the honorary passport applies, you may come into possession of information concerning the private affairs of patients, the general public or of employees and students of other Founders. Such information must always be treated as confidential. Breach of confidentiality will be regarded as a reason for terminating your placement and may also be treated as a disciplinary offence under your substantive contract of employment. You will also be required to adhere to the Data Protection Act 1998.

3.7. You are required to wear any security badge, name badge and uniform provided in accordance with the requirements of the Founder where you are working.

3.8. If, due to sickness, or for any other reason, you are unable to attend your work, you must inform, in addition to your substantive employer, your supervisor at the Founder and your placement organiser as soon as possible.

3.9. If you are already employed by a Founder, all of your pre-employment checks; occupational health, identity, CRB/ISA registration, employment history & references, right to work, professional registration and qualifications; are valid in the Host organisation providing that duties of a similar nature are being performed. In the event that you are required to undertake different duties or are not substantively employed by a Founder with existing checks in place, you may need to undergo relevant employment checks in accordance with the requirements of the Founder policies and procedures at whose site you are performing duties under the honorary passport.

3.10. You are indemnified from any legal claims arising from the proper execution of your responsibilities with the Founder with whom you hold the honorary passport, provided that they are not attributable to any negligence or misconduct on your part.

3.11. The Founder with whom you hold the honorary passport will grant you access to its facilities such as library, social club, meals, etc on the same basis as its employees, subject to availability.

3.12. In the course of your duties with any Founder member organisation, and while using Founder facilities, should you make any invention or other original work, no arrangements may be made with outside bodies to exploit this invention without the express permission of that Founder. This covers all activities associated with this honorary role unless a separate agreement on Intellectual Property Rights is in force between the Founder for whom you are performing your honorary duties and your substantive employer.

3.13. It is a condition of the honorary passport that all ***academic*** publications including those related to clinical innovation will cite King's College London as the research centre where this work was primarily focused. The citation should be consistent with King's College London's current citation policy

3.14. If you have a grievance against the Founder with whom you hold the honorary passport or any of its employees, you should raise this informally in the first instance with the person to whom you report at the Founder. Should the matter not be resolved and you wish to raise a formal grievance you should do so with your substantive employer under its grievance policy.

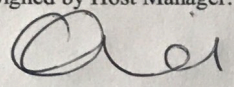
3.15. The Founder with whom you hold the honorary passport reserves the right to suspend the honorary passport and require you to leave the work area, or to terminate your honorary passport if, in the opinion of management, you are unfit to continue the honorary passport or have seriously breached organisation rules. Your substantive employer will be informed of any such issues and this may also lead to disciplinary action by your substantive employer under its disciplinary policy.

3.16. The honorary passport can be varied or amended to reflect the needs of the service, subject to agreed procedures and you will be advised of any changes by way of general notice to all members of staff and the date that such changes will take effect.

Honorary Passport Validation

Name:

You must identify the Host Line Manager to whom you are responsible at ***every*** designated site you work within King's Health Partners. It is your responsibility to obtain their sign-off.

Host Institution: * GSTT / KCH / SLAM / KCL ** circle one*	
Valid from: 19/12/19	End date: 22/05/20
Name of Host Manager: ELLIE. RASHID.	
• Signed by Host Manager:  Date: 19/12/19	

Host Institution: * GSTT / KCH / SLAM / KCL ** circle one*	
Valid from:	End date:
Name of Host Manager:	
• Signed by Host Manager: Date:	

Host Institution: * GSTT / KCH / SLAM / KCL ** circle one*	
Valid from:	End date:
Name of Host Manager:	
• Signed by Host Manager: Date:	

- ***By signing this Honorary Passport I accept responsibility and activities of the above named whilst undertaking work within the Host Institution***

Please note that additional copies of this signatory page may be added if required for additional honorary placements.